THE

ETIOLOGY AND NATURE

OF

CANCEROUS AND OTHER GROWTHS.

W. T. GIBSON.

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THE ETIOLOGY AND NATURE
OF
CANCEROUS AND OTHER GROWTHS

BY

W. T. GIBSON, A.R.C.S.

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PREFACE.

MY interest in this subject was aroused during the study of asexual reproduction, for cancerous growth seemed to be a related phenomenon. But I am now convinced that, though there is a superficial resemblance, this line of attack is a wrong one. Groping in the darkness, I followed many will-o'-th'-wisps until I gained possession of a table showing the incidence of cancer in certain occupations. So pronounced were the differences shown, it was clear that part of the solution of the mystery lay behind, though some time elapsed before it was found.

This work is of the nature of a preliminary statement, made in the hope that in the course of time it will be followed by a more extensive work. A vast amount of the literature is yet to be examined at first-hand, and some general statements made in various works need to be traced to their sources. And as I am quite unable to form an estimate of the time when some degree of finality may be reached, it has seemed best to give part of my results in their present form. It will be noted that my work constitutes an *ex parte* statement, but discrimination has been exercised in the adoption of statements having the appearance of rashness.

There are a number of reasons for my omission as yet to give references to the sources of information.

Whatever may be the reception given to the line of argument adopted and to my interpretation of the evidence, there will otherwise be a use for this book, for it brings together in a more complete manner than usual certain evidence bearing upon the etiology and nature of neoplasms.

I have not confined myself to the study of cancerous growths, but wander indifferently among the sarcomatous and innocent.

Few will deny the probability that up to a certain point the conditions necessary for the development of all forms of neoplasm are the same ; and this probability is strengthened in the course of this work. Malignancy seems to depend considerably upon the shape of the cells which proliferate abnormally, and upon whether they belong to a compact tissue or to an epithelium. It is denied to a feltwork of elongated cells. How far the shape of the cells is responsible can be understood when the respective malignancy of round-celled and spindle-celled sarcoma is compared.

Dermoid cysts are not considered for the reason that they appear to be formed by vagrant germ-cells developing parthogenetically, and are in quite a different category to the tumours proper.

The general term cancer is used somewhat indifferently in the following pages, but the more exact terms are used where they are given by the authorities consulted.

Some of the matter in Chapters XXII. and XXIII. has already been published anonymously in pamphlet form, but here it receives a severe editing and a more rational setting.

My gratitude is given to those who have helped me to gain facilities in consulting the literature.

W. T. GIBSON.

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TABLES SHOWING THE OCCUPATIONAL INCIDENCE OF CANCER, &c.

THE following tables are based upon tables given by Dr. Tatham in the Decennial Supplements to the 55th and 65th Annual Reports of the Registrar-General for England and Wales. I have altered the order of the occupational groups to correspond with the order of the relative incidence of cancer. The comparative mortality figure from alcoholism and for all causes is given : why, will later be learnt. In the last column of each table are shown the number of deaths from cancer in each occupational group. This is to serve as a guide to the reliability of the comparative mortality figure for cancer, for where the number of deaths is small, slight adventitious causes affecting the death-rate from cancer may induce undue abnormality of this comparative mortality figure. Upon this point the tables constitute a powerful object-lesson. For the purpose of simplicity, and for other reasons, certain subsidiary or unimportant groups appearing in the original tables have been omitted. The statistics refer to deaths between the ages of 25 and 65. Deaths of individuals who had retired are not included.

TABLES SHOWING THE OCCUPATIONAL

Table I.—1890-2.

Occupation.	Comparative Mortality Figure.			Total Number of Deaths from Cancer.
	Cancer.	Alcoholism.	All Causes.	
Chimney Sweep, Soot Merchant	180	69	1516	45
Copper Miner	99	—	1423	3
Tallow, Soap, Glue, Manure, &c., Manufacturer	84	—	1282	15
Brewer	81	48	1649	63
Inn, Hotel Servant	75	122	1997	37
Slater, Tiler	73	18	1527	15
Commercial Traveller	72	26	1111	89
Law Clerk	71	25	1237	29
Plasterer, Whitewasher, Paperhanger	71	17	1256	61
Currier; Leather Goods—Maker, Dealer	70	11	1154	41
Barrister, Solicitor	69	15	950	45
Maltster	69	17	1021	21
Merchant Seaman	69	25	1564	191
Bookbinder	69	18	1225	16
Gasworks Service	68	8	1246	63
Coach and Cab Service, Groom, &c.	67	32	1334	289
Carman, Carter, &c.	67	20	1484	249
Milkseller, Cheesemonger, &c.	67	20	1225	52
Tool, Scissors, File, Saw, Needle—Maker	67	14	1633	72
Sawyer	67	12	889	53
Stone, Slate—Quarrier	67	9	1359	101
Butcher	66	39	1267	125
Gunsmith	66	33	1419	18
Coalheaver	64	34	1765	32
Glass Manufacturer	64	26	1719	28
Rope, Twine, Cord—Maker	63	6	1075	13
Chemist, Druggist	63	21	1071	31
Manufacturing Chemist	63	8	1609	33
Innkeeper, Publican: Wine, Spirit, Beer—Dealer	61	106	1899	208
Plumber, Painter, Glazier	61	15	1295	255
Tinplate Manufacturer, Tinplate Goods Maker	60	11	1148	41
Textile Dyer, Bleacher, &c.	60	12	1585	50
Brass, Bronze—Worker	59	11	1257	35
Publisher, Bookseller, Stationer, &c.	59	12	963	35
Tobacco Manufacturer, Tobacconist	59	29	1159	22
Dock Labourer	59	60	2114	103
Shoemaker	58	11	1064	347
Coach, Carriage—Maker	58	11	1201	53
Tin Miner	58	4	1628	12
Draper	57	16	1174	65
Wool, Worsted—Manufacturer	56	3	1146	115
Lead Miner	56	5	1514	11

XI.

INCIDENCE OF CANCER, &c.

Table II.—1900-2.

Occupation.	Comparative Mortality Figure.			Total Number of Deaths from Cancer.
	Cancer.	Alcoholism.	All Causes.	
Chimney Sweep	136	45	1240	38
Brewer	112	46	1324	87
Furrier, Skinner	111	23	1274	19
General Labourer	111	40	1987	1420
Merchant Seaman	103	26	1547	285
Tinplate Manufacturer, Tinplate Goods Maker	95	10	974	72
Inn, Hotel Servant	88	129	1767	45
Manufacturing Chemist	85	4	1031	57
Lead Worker	82	38	1385	6
Indiarubber, Guttapercha Worker ; Waterproof Goods Maker	82	11	971	20
Boiler Maker	82	12	971	94
Wood Turner, Cooper, &c.	80	31	1104	86
Textile Dyer, Bleacher, &c.	79	11	1066	90
Costermonger, Hawker, Streetseller	79	57	1778	112
Messenger, Porter, &c. (not Railway or Government)	79	32	1341	150
Lace Manufacturer	79	8	831	23
General Shopkeeper	78	43	1421	63
Cabinet Maker, French Polisher, &c.	75	15	888	192
Bargeman, Lighterman, Waterman	75	15	1235	71
Coach and Cab Service, Groom, &c.	74	29	1062	397
Tailor	74	13	953	263
Hosiery Manufacturer	74	5	853	32
Corn Miller	73	8	842	52
Musician	73	36	1140	44
Law Clerk	72	8	880	37
Bookbinder	71	16	889	21
Carman, Carter, &c.	71	18	1094	397
Gunsmith	71	18	1087	21
Baker, Confectioner, Pastrycook	70	12	852	156
Zinc Worker	70	15	889	4
Gasworks Service	69	9	838	102
Lead Miner	69	6	1199	10
Barrister, Solicitor	69	13	739	56
Cotton, Linen, &c., Manufacturer	69	11	1037	254
Plumber, Painter, Glazier	69	12	1041	399
Currier ; Leather Goods—Maker, Dealer	68	9	944	44
Butcher	68	31	1062	145
Tin Miner	68	—	2169	10
Artist, Engraver, Sculptor, Architect	68	18	760	42
Commercial Clerk, Insurance Service	68	11	837	394
Physician, Surgeon, General Practitioner	67	17	952	55
Commercial Traveller	67	21	907	119

TABLES SHOWING THE OCCUPATIONAL

TABLE I. *(continued)*.—1890-2.

Occupation.	Comparative Mortality Figure. Cancer.	Alcoholism.	All Causes.	Total Number of Deaths from Cancer
General Labourer	55	16	1413	821
Copper Worker	55	4	1597	11
Engine, Machine—Maker, Fitter	55	12	1256	172
Messenger, Porter, &c. (not Railway or Government)	55	18	1415	97
Railway Platelayer, Road Labourer, Navvy, &c.	54	12	1221	190
Printer	54	12	1267	68
Saddler	53	18	1069	33
Nail, Chain, &c., Manufacturer	53	14	1504	258
Zinc Worker	53	22	1381	4
Musician	53	34	1404	27
Fisherman	53	4	976	34
Railway Engine—Driver, Stoker	53	2	934	32
Tailor	52	14	1144	178
Corn Miller	52	5	974	35
Bargeman, Lighterman, Waterman	52	19	1386	45
Bricklayer, Mason, Builder	52	11	1157	408
Costermonger, Hawker, Streetseller	52	42	1911	69
Baker, Confectioner, Pastrycook	52	13	1061	103
Locksmith, Gasfitter	52	11	1069	28
Blacksmith, Whitesmith	52	11	1057	205
Carpet, Rug—Manufacturer	52	—	1010	12
Coal, Coke—Merchant; Coke, &c., Burner.	51	15	929	56
Brick, Tile—Maker, Burner	51	10	857	52
Cabinet Maker, French Polisher, &c.	51	17	1131	102
Boiler Maker	51	11	1162	41
Carpenter, Joiner	50	9	905	333
Physician, Surgeon, General Practitioner	50	16	1118	31
Watch, Clock, Instrument, &c., Maker	49	11	1130	76
Hatter, Hat Manufacturer	49	27	1283	15
Silk, Satin, &c., Manufacturer	49	10	1064	24
Railway Guard, Porter, &c.	49	6	953	102
Fishmonger, Poulterer	48	33	1115	33
Artist, Engraver, Sculptor, Architect	48	12	900	23
Wood Turner, Cooper, &c.	48	21	1258	42
General Shopkeeper	47	15	1126	43
Ironmonger, Hardware Dealer	47	14	933	21
Commercial Clerk, Insurance Service	47	14	1056	184
Cotton, Linen, &c., Manufacturer	46	11	1318	158
Schoolmaster, Teacher, &c.	46	9	698	42
Ship, &c., Builder	45	10	836	79
Hairdresser	45	40	1270	17
Domestic Indoor Servant	45	20	876	36
Railway Official, Clerk	44	6	904	39

TABLE II. *(continued).*—1900-2.

Occupation.	Comparative Mortality Figure.			Total Number of Deaths from Cancer.
	Cancer.	Alcoholism.	All Causes.	
Dock Labourer	67	49	1374	200
Watch, Clock, Instrument, &c., Maker	67	8	817	145
Tool, Scissors, File, Saw, Needle—Maker	67	9	1231	81
Nail, Chain, &c., Maker	66	12	1137	366
Innkeeper, Publican; Wine, Spirit, Beer—Dealer	66	105	1669	251
Fisherman	66	12	892	48
Shoemaker	66	12	901	385
Blacksmith, Striker	66	11	884	266
Domestic Indoor Servant	65	13	815	59
Hatter, Hat Manufacturer	65	6	1046	25
Slater, Tiler	64	14	1036	17
Plasterer, Whitewasher, Paperhanger	64	26	937	77
Carpet, Rug—Manufacturer	64	5	942	12
Potter, Earthenware Manufacturer	63	7	1420	51
Printer	63	8	935	111
Wool, Worsted—Manufacturer	63	7	927	136
Glass Manufacturer	62	7	1202	34
Rope, Twine, Cord—Maker	62	5	826	12
Tallow, Soap, Glue, Manure, &c., Manufacturer	62	4	689	15
Brass, Bronze—Worker	62	10	1074	51
Carpenter, Joiner	62	13	769	491
Stationery Manufacturer; Stationer, Publisher, Newsagent	61	18	872	80
Maltster	60	12	734	18
Greengrocer, Fruiterer	60	22	882	71
Railway Guard, Porter, &c.	59	6	773	191
Fishmonger, Poulterer	58	24	943	47
Engine, Machine—Maker, Fitter	58	9	848	392
Milkseller, Cheesemonger, &c.	57	12	776	69
Hairdresser	57	20	1070	27
Bricklayer, Mason, Builder	57	13	862	636
Coalheaver	57	30	1144	45
Ironmonger	55	11	700	32
Chemist, Druggist	54	24	934	33
Tobacco Manufacturer, Tobacconist	54	42	898	27
Draper	54	12	755	72
Coach, Carriage—Maker	54	4	774	73
Sawyer	53	13	717	46
Ship, &c., Builder	53	9	765	137
Stone, Slate—Quarrier	53	6	905	112
Brick, Tile—Maker, Burner	53	9	622	72
Railway Official, Clerk	52	6	707	75
Grocer, &c.	52	9	670	167

TABLES SHOWING THE OCCUPATIONAL

TABLE I. *(continued).*—1890-2.

Occupation.	Comparative Mortality Figure.			Total Number of Deaths from Cancer.
	Cancer.	Alcoholism.	All Causes.	
Ironstone Miner	44	4	893	21
Greengrocer, Fruiterer	43	21	1093	40
Tanner, Fellmonger	43	9	873	13
Gardener, Nurseryman, Seedsman	42	4	638	248
Farmer, Grazier, &c.	42	7	651	454
Coal Miner	42	5	1068	412
Farm Labourer, Farm Servant	41	4	731	888
Clergyman, Priest, &c.	41	1	615	65
Potter, Earthenware Manufacturer	40	10	1970	26
Grocer, &c.	39	9	768	119
Wheelwright	39	10	899	32
Hosiery Manufacturer	35	9	808	20
Lace Manufacturer	33	3	819	10
Lead Worker	31	—	2061	2
Paper Manufacturer	25	9	1043	6
All Occupied Males	51	15	1102	11468
,, ,, (London)	68	20	1325	2098
,, ,, (Industrial Districts)	55	22	1443	2538
,, ,, (Agricultural Districts)	46	8	795	1702

INCIDENCE OF CANCER, &c.

TABLE II. *(continued).*—1900-2.

Occupation.	Comparative Mortality Figure.			Total Number of Deaths from Cancer.
	Cancer.	Alcoholism.	All Causes.	
Ironstone Miner	52	6	723	27
Coal Miner	51	5	846	700
Silk, Satin, &c., Manufacturer	51	14	892	15
Saddler	51	12	889	39
Farmer, Grazier, &c.	51	8	562	576
Schoolmaster, Teacher, &c.	49	6	599	61
Clergyman, Priest, &c.	48	2	515	92
Railway Platelayer, Road Labourer, Navvy, &c.	48	6	707	289
Gardener, Nurseryman, Seedsman	48	5	527	344
Railway Engine—Driver, Stoker	48	3	582	60
Farm Labourer, Farm Servant	45	6	572	744
Coal, Coke—Merchant; Coke, &c., Burner	42	17	695	55
Locksmith, Gasfitter	41	11	890	25
Wheelwright	40	6	757	35
Copper Miner	39	48	1609	1
Paper Manufacturer	39	2	684	13
Copper Worker	39	7	1041	11
Tanner	33	11	737	9
All Occupied Males	63	16	925	16655
,, ,, (London)	86	24	1099	3082
,, ,, (Industrial Districts)	68	18	1129	4488
,, ,, (Agricultural Districts)	51	10	670	2228

THE
Etiology and Nature of Cancerous and other Growths.

CHAPTER I.

Local Irritation as a Cause of Abnormal Growth.

THOUGH abnormal growth can be ascribed in some cases to local irritation—to inflammatory conditions, and to chemical, mechanical, and other forms of trauma—in most cases evidence of this nature is absent. Yet a number of considerations may be advanced to weaken this negative evidence. Memory is short, while cancer, for example, may supervene the span of an ordinary lifetime after a lesion. We do not know what is the minimum degree of irritation necessary to induce cancer. In the case of the skin, the effects may be imperceivable, for the epidermis is resistant to, and it may even be stimulated to excessive growth by irritation when the dermis below it is damaged. It is difficult to explain the occurrence of multiple neoplasms, say, the multiple lipomata which appear in the victims of alcoholism, without assuming the potency of an irritant in the blood. We must further keep in mind the possible potency of an irritation of reflex origin, or, as the work of Cheatle suggests, irritation due to inflammatory conditions in the nerve-centres. The usually isolated occurrence of cancer is an important fact which is explicable as the result of irritation.

While direct evidence of precancerous irritation is available only in a minority of cases, the indirect evidence is very strong, and is here partly recapitulated.

Cancer occurs most frequently in regions of the body exposed the most to irritation. Men suffer more than women from cancer of exposed surfaces, while the incidence in both sexes is approximately equal in organs which are not liable to special forms of irritation. Cancer of the lip much more rarely occurs in women than in men, and the women are frequently smokers. In men it is generally the lower lip which is attacked, while the frequency in the upper lip is about the same for both sexes. Owing to habits of spirit-drinking and smoking, and as a result of the nature of some occupations, the large majority of sufferers from cancer of the tongue, throat, and œsophagus belong to the male sex. The commonest sites of cancer of the œsophagus are those places where it is narrowed, where there must be considerable friction as the bolus passes. The alimentary canal is most frequently cancerous in the parts most subject to irritation, as in the stomach and large intestine. In the colon the incidence is greatest at the flexures, where are to be expected putrescence and delay in the passage of fæces and the irritation of scybalæ. Cancer of the rectum occurs in about 80 per cent. of intestinal cases. To cancer of the gall-bladder, and its common precursors—gall-stones—women are about three times as prone as men. In both sexes the age of greatest liability—50–60 years—is the same for these two diseases. The uterus and mammæ—organs very much exposed to irritative conditions—are the most frequently attacked in women. There is more evidence of this nature.

In the case of sarcoma the direct evidence of irritation in the form of injury is very strong. It occurs most commonly when the most active existence is led, before middle life is reached. Sarcoma of the breast is reported mostly in young married women, and is rare after the age of forty.

Among the innocent tumours keloid—using the term in the broadest sense—is the most significant example.

Though in the following chapters the case for a traumatic origin of cancer will be further strengthened, facts do not justify the assertion that traumata are the only agents, but this is a matter into which we cannot yet enter.

CHAPTER II.

OCCUPATIONAL INCIDENCE. OCCUPATIONS CONCERNED WITH HEAT DECOMPOSITION PRODUCTS. SMOKING.

I WILL begin by drawing attention to the enclosed tables, which are based upon data given by Dr. Tatham in the two last Decennial Supplements to the Registrar-General's Annual Reports. Occupational groups are in them arranged in order corresponding to the incidence of cancer in the respective periods 1890–2 and 1900–2. (*See* pp. IX.–XV.)

In the upper part respectively of each table it will be seen that there predominate occupations in the course of which the workers come into contact with organic compounds—gaseous, liquid, and solid—the result of the combustion and destructive distillation of coal, and the decomposition of animal matter by heat and by putrefaction, while coming under the same category (as will later be made clear) are the occupations concerned in the manufacture and sale of alcoholic liquors. Occurring about the top of the table dealing with the first period are the following: chimney sweep, soot merchant; tallow, soap, glue, manure, &c., manufacturer; brewer; inn, hotel servant; currier, &c.; maltster; gasworker; coach and cab service, groom, &c.; carman, carter, &c.; butcher; innkeeper, publican, &c. The bottom of the table is free of occupations coming under this category, with one exception—tanner, fellmonger. The above feature is not so pronounced in the other table, in which some of these occupational groups occupy a lower position, yet it is observable in the case of the following: chimney sweep; brewer; furrier, skinner; inn, hotel servant; indiarubber, &c., worker (carbon bisulphide and naphtha being used in rubber factories). The other occupational groups mentioned above come not far behind. The tanner (some of the fellmongers being now grouped with the tanners, the remainder are included in other groups) is in the lowest position, yet otherwise the lowest part of the table is again free.

In the sequel it will be shown that organic decomposition products play a part in the case of other occupational groups occupying a high position in the table which would not at a first glance be placed in the above category. In yet others we must look in another direction for the causative agents. But in the meantime we had best confine ourselves to certain occupational groups of the nature above indicated, leaving the others for later consideration. In attacking the cancer problem I have crept from position to position, and the expounding of my case will best follow the same course. It is a natural method for which I cannot find a substitute.

After the name of each occupational group below are given the comparative mortality figures during both periods for cancer and alcoholism. In the case of each disease the first and third numbers are the figures, for the first and second periods respectively, showing the comparative mortality in the occupational group; the second and fourth numbers, within parentheses, are the figures for "all occupied males," and are given in every case to facilitate comparison. The comparative mortality figure for alcoholism is given because it is clear that alcoholic liquors play a part in causing cancer, though the death-rate from alcoholism is only a partial guide to the degree of intemperance.

Chimney Sweep, Soot Merchant [*Cancer*—180 (51), 136 (63); *Alcoholism*—69 (15), 45 (16)].

Epithelioma of the scrotum is commonly known as "chimney sweep's cancer," and is preceded by soot-warts or eczema. It has long been agreed that some potent constituent of the soot is dissolved out by the sweat, and that decomposition of the latter and friction of the clothes also help. Butlin states that the incidence among Continental sweeps is lower in those countries where greater cleanliness is practised among them, as by daily bathing and the wearing of specially-designed and frequently-changed apparel. Scrotal epithelioma is almost unknown in countries where wood is used as fuel, and the soot from hard (stone) coal is more dangerous than that from brown coal (lignite). Where coke and anthracite are consumed, the incidence is small, for these fuels form little soot. To epithelioma of the hands and forearms soot merchants are liable, and also are gardeners who have frequently to spread soot. A case of epithelioma is reported in a gardener who habitually carried a bag of soot over the arm, and was there attacked.

We can gain only a partial knowledge of the substances contained in soot, though a guess may be made at their general nature. Professor Knecht has made the most detailed examination of soot, which he obtained from Manchester dealers. An aqueous extract was strongly acid owing to the presence of free sulphuric acid. It contained ammonia and pyridine bases, while ammonium sulphate and chloride were also present. In a sulphuric acid extract was calcium sulphate, and the filtrate, of a light brown colour, contained compounds of the basic constituents. A caustic soda extract was a dark brown liquid, from which the acid constituents were precipitated with dilute sulphuric acid. These were of a brown colour, and charred on heating, with evolution of a little gas, not melting nor volatilising. They appeared to resemble the indefinite organic substances classed as humic acid. A benzene extract consisted mainly of hydrocarbons with a high boiling-point. An estimate of the composition of the soot was made as follows :—

Ammonium sulphate	10·7
Mineral matter	19·6
Acid constituents	10·9
Benzene extract	13·0
Difference (carbon ?)	45·8
	100·0

I am unable to co-ordinate exactly the information given in the table with that in the text. Knecht remarked that the smell of soot had been ascribed to the pyridine bases, but he was not aware of the experimental basis for this assumption. This smell pervaded all the extracts, and was more akin to the odour of humus, or to the peculiar odour given off from the earth after a shower of rain preceded by dry weather.

Voelcker found alkaline salts and calcium and magnesium carbonates in commercial soot. There is arsenic in soot.

The high death-rate from alcoholism among sweeps should be noted.

Gasworks Service [*Cancer*—68 (51), 69 (63) ; *Alcoholism*—8 (15), 9 (16)].

In the case of the gasworker, though he may be attacked by epithelioma of the scrotum, evidence is not available of its frequency compared with cancer in other organs, so that we cannot determine how far the gaseous products are responsible. But for the reason that, as will be shown later, gaseous substances from other sources are entitled to suspicion, the gases formed by the destructive distillation of coal will be recounted. Tar distillation is carried on in large gasworks, and tar is a potent agent, as are some of its constituents, and even pitch is an agent.

A journey on the leeward side of a gasworks will afford some proof of the emanations to which the worker is exposed. Leakages of smoke and impure gas take place in the retort-house. Obnoxious effluvia arise during the process of emptying the purifiers and from the spent lime deposited in the yard, from the exposure of tar and ammoniacal liquor to the air, and during the removal of spent lime, tar, and liquor from the premises. There will be a certain amount of personal contact with the three latter substances, and, where tar is distilled, with the compounds isolated.

In unpurified coal gas are present various hydrocarbons (ethylene, propylene, acetylene, methane, benzene, naphthalene), carbon monoxide and dioxide, hydrogen and carbon bisulphides, sulphur dioxide, ammonia, hydrocyanic acid or ammonium cyanide, and sulphocyanogen. In ammoniacal gas liquor have been identified ammonia and some of its salts, members of the pyridine series, phenols and sulpho-acids, and sulphocyanogen and other sulpho-compounds and cyanides. Coal-tar contains a great range of substances, many of which have not been properly identified, especially those with a high melting-point. Hydrocarbons are numerous, and the phenols and compounds of cyanogen are familiar. Among the nitrogenous bases are members of the pyridine, quinoline, and acridine series, aniline, &c., and, among other nitrogenous compounds, pyrrol and carbazol. In the part of the tar which remains to form pitch, after the oils have been extracted by distillation, are hydrocarbons with a high melting-point (anthracene, chrysene, &c.), the higher members of the quinoline series and members of the acridine series. There are stable nitrogenous compounds in hard pitch even which are not yet identified. Sulphur compounds are also present. It has been suggested that fatty amines are present in coal-tar, but there does not seem to be any definite evidence. They are found in wood-tar.

Indiarubber, Guttapercha—Worker : Waterproof Goods Maker [*Cancer*—82 (63) ; *Alcoholism*—11 (16). 1900–2 *only*].

The workers in this occupational group suffer severely from the fumes of naphtha and carbon bisulphide, which are solvents of rubber and vulcanising agents.

Among the workers in allied occupations a relation has been proved between heat decomposition products and cancer. In tar distilleries, shaleworks, and petroleum or naphtha refineries those employed are liable especially to cancer of the hands and forearms and of the scrotum, following warts and various forms of dermatitis. Multiple cancer of the face, preceded by seborrhœa, is not infrequent, and even the eyelids are prone to attack.

In the case of the shaleworkers Kirk reported that the miners and retort-men were generally exempt, most of the cases occurring among the men employed in refining the paraffin-wax, but the incidence was lessened when superheated steam began to be used in purification. Previously, naphtha was used, and the workers' hands and forearms were constantly in contact with the naphtha mixture. As a result, intractable eczema was common, and boils would form. Instead of healing, sometimes the boils developed into very indolent ulcers, and sometimes these ulcers eventually displayed malignancy. A worker who did not wear the leather apron provided, having his trousers, therefore, constantly soaked with the naphtha mixture, contracted eczema of the scrotum, and in course of time epithelioma.

Ammonia, members of the pyridine and quinoline series, aniline, pyrrol, and various acids, in addition to the essential hydrocarbons, have been identified in the light oils (variously and indifferently named naphtha, paraffin, &c.) extracted from coal-tar and the distillate of shale. In the shale-oil are also nitriles of the fatty acids. But it is certain that this list is not exhaustive. During the process of refining light oils are removed some of the more easily explosible hydrocarbons and basic and acid impurities.

Reporting upon 39 cases of scrotal cancer—of which 29 occurred in sweeps—Butlin pointed out that of the ten patients remaining six came into contact with tar in the course of their employment.

Men employed in the pounding or grinding of pitch suffer from a cancroid eruption of the skin which is described as being similar to that of chimney sweeps.

The workers in a French factory where patent fuel is made from coal dust and pitch appear to suffer freely from cancer. The binding agent of the fuel is not mentioned. Many different kinds of material, including tar and mineral oils, are used in these factories as binding agents.

Oliver recorded cases of epithelioma on the hands and forearms in mineral (waggon) grease workers. The essential constituents of mineral grease, which is prepared from coal-tar and is mixed when hot, are hydrocarbons, mostly semi-solid, but impurities such as are found in naphtha must be present.

A patient of Mackenzie's, who worked among (coal-tar ?) creosote for 30 years, had comedones on the hands and forearms, and between them wart-like growths. Similar growths upon the scrotum became epitheliomatous. There is recorded a case of cancer of the tongue developing in a scar left after the application of (wood-tar) creosote.

Rehn drew attention to the frequent occurrence of growths (papillomata) in the bladder, which finally became malignant, among the workers in chemical factories, especially where fuchsine is made from aniline and toluidine. Vapours evolved during the manufacture of the fuchsine were blamed. The presumption is that the aniline and toluidine were inhaled, and, passing through the body unchanged, which is known to be the case with aniline, were excreted in the urine, when they induced the formation of the neoplasms.

Leichtenstein, describing irritative conditions of the bladder, against which free ventilation was a prophylactic, among workers employed in factories where aniline was made from nitrobenzene, toluidine from nitrotoluene, and these substances were used in the production of fuchsine, mentioned two cases of neoplasm of the same organ. In one case aniline is given as the specific irritant, but it is mentioned that toluidine as well as aniline is especially liable to irritate the bladder.

In the Glasgow hospitals McCall Anderson and others noted a large number of cases of epithelioma, especially of the face and mouth, in poor elderly people of both sexes coming from the Hebrides and Western Highlands of Scotland. Peat smoke was suggested as the causative agent.

Now, especially in the causation of cancer of the tongue, and, in a less degree, in cancer of the throat, tobacco-smoking plays a part, though in the case of cancer of the tongue the claim is sometimes made that the effects of the smoke are merely superadded to the effects of syphilis.

A pipe may be described, somewhat pedantically, as an instrument for the destructive distillation of tobacco. Tarry matter, and nicotine also, is condensed in the stem. In the smoke have been identified nicotine, most of the members of the pyridine series, methylamine, ethylamine, pyrrol, ammonia and ammonium carbonate and acetate, acetic and butyric acids, phenol, hydrocyanic acid, formaldehyde, hydrogen bisulphide, carbon dioxide and monoxide, and hydrocarbons.

There is evidence to show that nicotine is an agent, and it had best be considered here. Dennis, in Langenberg's clinic in Berlin, saw cases of epithelioma of the cheek which was there called " American disease " because it was chiefly seen among those who chewed tobacco. Butlin suggests that the chewing of tobacco, kept always in the same place, may induce cancer of the tongue. Cancer of the lip occurs in cigar-smokers, and may be due to the action of nicotine, which can pass through the skin, but it is impossible to exclude the action of tarry products condensed in the stump.

Tobacco Manufacturer, Tobacconist [*Cancer*—59 (51), 54 (63) ; *Alcoholism*—29 (15), 42 (16)].

The workers in this occupational group receive the credit of being inveterate smokers, and, as might be expected, they are especially prone to the attack of tobacco dust, yet the incidence is not very high.

CHAPTER III.

OCCUPATIONS CONCERNED WITH ANIMAL MATTERS. DECOMPOSITION IN THE BODY. CANKER OF HORSES.

Tallow, Soap, Glue, Manure, &c., Worker [*Cancer*—84 (51), 62 (63) ; *Deaths from Alcoholism Practically Absent*].

THE high incidence during the first period justifies the inclusion of this occupational group, though certainly the total number of deaths from cancer during both periods was small, and the statistics are therefore not too reliable.

The emanations from works where these occupations are followed have long been matters of discussion among hygienists. In the case of glueworks particularly it is noted that the odours travel far afield, which is another way of stating that they are very pungent. Though nowadays the public authorities are less tolerant of offensive odours, so that the manufacturers are compelled to adopt palliative measures, and methods which are less objectionable, the workers whose deaths are recorded in the two reports lived partly during more tolerant times.

In tallow-rendering works there is putrefaction of the raw material, and the floors and walls tend to be filthy. According to the older method of rendering—now only followed in smaller works—the raw material was heated in coppers upon the bottoms of which the fires played directly. Previous treatment of the material with sulphuric acid lessens the odour during heating, which is otherwise considerable. This odour is not only due to the expulsion of volatile products of putrefaction, but is also the effect of charring at the bottom of the copper. Heating by steam is the newer method, when the odour is less offensive. Of course odour is only a partial guide to the degree of decomposition and to the extent to which volatile organic products pass into the air, but it is at present our only guide. After running off the melted fat, the residue is subjected to pressure for the extraction of the remainder of the fat, when there are further emanations. The extracted fat has a stale and putrid odour, and may become worse in this respect when stored. The material left after the extraction of the fat—the greaves—accumulates in the stores and may become very offensive.

I expect that workers in establishments where fish oils are rendered are included in this occupational group. Very offensive raw material is often used, and the emanations during the process of rendering in fire-heated coppers appear to be more offensive than when tallow is rendered.

In soapworks offensive odours arise when strong-smelling fat is melted out of the casks with steam. Also offensive are the operations of refining and bleaching the tallow, and soap-boiling itself. After the latter operation is completed—steam has now replaced direct heating—the soap is at the top of the copper, the caustic lye is at the bottom, and in the middle is a dark-coloured liquid containing organic impurities. Tallow, with some of the vegetable oils, is the least offensive of the materials used, and for the cheaper soaps, especially those used in wool-scouring, are employed some putrid and foul-smelling oils and fats : bone tallow (a bye-product of bone-boiling), which may be dark-coloured as well as foul-smelling ; horse grease from tanneries ; Yorkshire grease (a product from the cleansing of sheeps' wool) ; and fish oils, which are sometimes exceedingly offensive. The bye-product glycerine is very impure at first owing to the presence of " empyreumatic compounds." During the storage of raw fats and oils " alkaline effluvia " are given off. It is worth mentioning that mineral oils appear in both vegetable and fish oils as adulterants, and that petroleum and tarry products are components of some medicated soaps, while petroleum and mineral grease are sometimes saponified.

Candle-making is a frequent adjunct to soap-boiling, and the raw material—paraffin scale from shale distilleries—is received in an impure condition, having a decided colour and smell, and evidently containing tarry compounds.

Glueworks are the seats of considerable putrefaction. Decomposing matter adheres to the walls and floors, and in the yards the raw material—the stock—is allowed to accumulate sometimes over an extended period. The putrefaction of the stock continues during the liming, a preliminary process lasting from eight to fourteen days. With the older method of allowing the fire to play directly upon the copper, charring was inevitable, though it was considerably lessened by the use of a perforated false bottom upon which rested the stock. Boiling is now performed in a copper with a water (or steam) jacket, or by means of a steam coil led inside, so that the emanations are less noxious. Prolonged boiling, or an excessive alkaline or acid reaction of the material leads to a greater degree of decomposition. When spread upon the nets to dry, the glue sometimes undergoes a sufficient amount of decomposition to become liquefied, so that a limited amount must take place as a rule. The finished article emits an odour when in the gluepot, and, indeed, some workmen prefer a dark and fœtid-smelling glue, such as follows from the use of putrid raw material or from prolonged boiling. Scutch—the material remaining after the extraction of the glue—is allowed to accumulate in the works until it becomes obnoxious, and one writer mentions its "ferocious, sickening smell."

Fish glue, made from the heads and tails, possesses a very disagreeable odour which requires to be masked with creosote.

As far as manure works are concerned, it is sufficient to recall that the raw material, where it is organic, is obtained from the most diverse sources. Detail is unnecessary. Some of it is in the form of trade waste. Gas liquor is a raw material.

The boiling of oil and varnish-making here included involve liberation of volatile fatty acids and the very offensive acrolein.

So many kinds of bacteria act upon organic substances of a varied nature that there must be a large range of compounds formed during putrefaction, and it can only be a minority of these which have been identified. Among the intermediate products are nitrogenous and non-nitrogenous fatty and aromatic acids, and many nitrogenous bases, such as fatty amines, aromatic amines (parvoline, isocollidine, &c.), and those ptomaines not answering to these descriptions. Ammonia, hydrogen bisulphide, methylmercaptan, and carbon dioxide are some of the simpler products. The fatty amines are stages in the transition to ammonia. The albumoses and peptones, and skatol and indol, must be mentioned for their possible potency. Some of the intermediate products as well as the simpler pass into the air, and while ammoniacal compounds (ammonia and fatty amines) make themselves evident in the effluvia, the offensively-smelling volatile fatty acids—propionic, butyric, caprylic, &c.—must not be forgotten. In putrefying glue have been found dimethylamine, isocollidine, neuridine, a muscarine-like base, and ammonia. Various compounds of phosphorus must be formed during putrefaction.

Complete evidence is not available of the decomposition products formed by the action of heat upon animal matter. Bone oil—formed by the destructive distillation of bones—may be considered a partly-efficient guide. In it are fatty amines, members of the pyridine series, acridine, aniline, other aromatic amines, and pyrrol. I am without information of the acids and other compounds present, but the oil cannot differ much from that obtained from coal and shale except, perhaps, in having a greater content of nitrogenous bases and a lesser content of hydrocarbons. From tallow in fire-heated open pans there escape into the air pyridine bases, ammonium cyanide, ammonium sulphide, hydrogen bisulphide, acetic and butyric acids, and acrolein, the latter being formed from charred fat. The following substances have been found in the dry distillate of gelatine : methylamine, butylamine, perhaps a trace of quinoline, and pyrrol and its derivatives. The heat and bacterial decomposition products in tallow are unidentified, but the animal oils will partly help us out of the difficulty. In cod-liver oil are fatty amines, dihydrolutidine, and morrhuene, along with free fatty acids, and in other animal oils have been identified fatty amines, pyridine bases, and pyrrol. This evidence leaves us somewhat in the dark, but it is sufficient to give a general idea of the nature of the compounds to the attack of which these workers are exposed.

Coach and Cab Service; Groom, &c. [*Cancer*—67 (51), 74 (63); *Alcoholism*—32 (15), 29 (16)]. *Carman, Carter, &c.* [*Cancer*—67 (51), 71 (63); *Alcoholism*—52 (15), 29 (16)].

In these occupations the men engaged are liable to come into contact with putrefying dung and urine, and to inhale their effluvia, the latter especially when entering the stables in the morning. The air, having been confined during the night, is then laden with decomposition products, with what is described as a peculiar ammoniacal smell, potent enough sometimes to induce symptoms of distress. Dung is allowed to accumulate for a long time in heaps outside and inside the stable, and urine percolates into the ground, while there may be pools formed by the urine and washings of the dung. Most of the individuals following these occupations can only suffer slightly in this way, and the most important factor is probably the frequency with which they reside above or in the immediate neighbourhood of the stables. Effluvia from stables are decidedly evident in the houses above. From the nature of their occupation these workers are less able to obey the calls of nature, so that there must be increased absorption into the blood of intestinal putrefactive products.

Ammonia is the only volatile product recorded in the case of putrefying urine, yet the bacillus ureæ can form trimethylamine from protein. In the case of manure there does not seem to be any reason for supposing that the intermediate and final products formed during its decomposition are very different from protein decomposition products. The intermediate products receive scant notice from the physiologist and agriculturist, upon whom we have to depend for information, and by the latter all nitrogenous bases appear to be returned as "free ammonia." In decomposing manure the most familiar compounds formed are ammonia and some of its salts, volatile fatty acids, and fatty amines. Skatol and indol, hydrogen bisulphide, and phosphuretted hydrogen are also formed. The odour of the amines is partly masked by that of ammonia, yet some of the former are themselves ammoniacal in odour. Methane is one of the products.

The death-rate from alcoholism is pronounced in these groups.

Butcher [*Cancer*—66 (51), 68 (63); *Alcoholism*—39 (15). 31 (16)].

In a meat salesman's shop free ventilation does not entirely dissipate the effluvia from the meat, which, of course, begins to decompose immediately after slaughter. During the early stages of decomposition meat has an acid reaction, but in the course of three or four days it has a faintly fœtid odour, and the reaction becomes alkaline owing to the predominance of ammonia and fatty amines. Slaughter-houses were once kept in a filthy condition, blood and scraps of flesh adhering to the walls and floors, the latter being also polluted with dung and urine.

Butchers naturally eat largely of meat, but I have been unable to find any indubitable evidence showing that meat-eating, excessive or otherwise, predisposes to cancer. Assertions to that effect are numerous enough. Butchers are said to suffer much from constipation, which will increase the absorption into the blood of putrefactive products.

The death-rate from alcoholism is again high.

Fishmonger, Poulterer [*Cancer*—48 (51), 58 (63); *Alcoholism*—36 (15), 18 (16)].

The relatively low incidence—just below the rate for "all occupied males"—is difficult to explain. Slaughter-house work is absent here, and, as far as fish is concerned, the stock is sold and replenished more quickly, so that putrefaction must be lessened. On the other hand game is allowed to attain a higher degree of putrefaction. The odour in the shops can seldom be considered obnoxious.

The leather and skin trades are discussed in a later chapter.

Now, cancer is relatively common in the large intestine compared with the small intestine, and especially in those localities (the rectum, the cæcum, and the flexures) where is to be expected putrescence of stagnant fæcal matter, though there must be also irritation by hard scybalæ. The bacterial decomposition products formed in the large intestine are supposed to differ to some extent from those formed outside of the body (from manure), owing to differences in the access to oxygen. Yet the differences cannot be very marked, for while the decomposition in manure heaps is putatively aerobic, volatile products formed in the manure must occlude the atmospheric elements, while oxygen percolating inwards must be rapidly used up. Otherwise we should expect the work of the bacteria to culminate in nitrification.

Naturally, it will be asked whether a history of constipation has been demonstrated in any cancer cases. I have searched without result among clinical records for evidence of this nature in cases of cancer in the intestine, and only in some few cases of cancer of other organs was my search rewarded. Dieffenbach, in his cases of cancer of various parts, found constipation in almost all. Having suggested constipation as a causative agent, George made inquiry among both cancer and other patients, but I am not clear about the result. Graves goes so far as to claim that he cured eight cases of epithelioma by administration of magnesium sulphate four times a day, though I am not inclined to place any dependence upon this statement. Constipation is apparently one of the causes of the formation of warts.

The liability of the stomach to become cancerous may be due in part to putrefactive products formed in the food before and after it enters the stomach.

Lyon examined the statistics of the American city of Buffalo, finding a very high death-rate from cancer among the German population, especially from cancer of the stomach. This was correlated by him with their peculiar diet. The pigs' fat used in sausage-making is by no means pure or fresh, and sausages may lie for a while before they are eaten. Of course, I would suggest decomposition products as the agents, though Lyon stands by the parasitic hypothesis.

The suggestion has been made that the ingestion of cheese is provocative of cancer. Now the maturation of cheese consists in a certain degree of decomposition, when fatty acids, ammonia, and fatty and aromatic amines form, whatever else there may be.

Snow pointed out that the special liability of the trigonal region of the bladder to cancer is referable to irritation by decomposing residual urine, and that an enlarged prostate, causing retention of urine, may lead to cancer of the bladder.

There is a disease of the feet of horses, known as "canker," which has not received notice in recent papers dealing with the subject of cancer in animals, and, though its parasitic nature has been asserted, in spite of failure to find a specific bacillus, it resembles so closely a cancerous growth that it deserves mention. Canker is an excessive growth of the epidermal layers of the foot, which, instead of making horn, form a "soft, unhealthy material, totally divested of elasticity, and devoid of all healthy resistance." This overgrowth develops into fungoid masses, and the process may involve the front and the sides of the foot, with the result that the hoof drops off. The only hope of cure is excision by the knife, followed by caustic or the cautery. Yet it may still recur, and sometimes it assumes a very malignant form, invading the coffin-bone and other parts of the foot, when the horse must be destroyed. This disease has the reputation of being a very intractable disorder. Horses kept in badly-tended stables are very liable to contract it, and the blame has long been attached to decomposing manure, urine, and moss-litter. At any rate, it is significant that canker rarely occurs in the fore feet, but is most frequently found in the hind feet. It is generally seen in heavy horses with weak, flat feet, creatures which proverbially receive but little grooming. Canker is said to be more prevalent in marshy districts than on dry highlands.

CHAPTER IV.

MISCELLANEOUS EVIDENCE IMPLICATING BACTERIAL DECOMPOSITION PRODUCTS. GOITRE.

A MASS of evidence has been accumulated which reinforces that already given. Some of it undoubtedly implicates bacterial decomposition products present in the air, and attention may be directed towards their potency when present in drinking-water. Continuous inhalation of obnoxious gases, and frequent ingestion of deleterious substances present in water, have appreciable physiological effects.

The incidence of cancer is greater in the neighbourhood of sewage farms and badly-kept manure heaps, and a higher death-rate has also been associated with sewage contamination of the soil. In the case of manure heaps, not only is there direct contamination of the air, but the washings percolate into the soil, and the gaseous products there formed pass into neighbouring houses. Foul air from a cesspool has been found to enter a house 27 feet away. Lloyd Jones thought that in Cambridge filth of all kinds—animal and vegetable—was present in the cancer districts.

To the composition of sewer air, which is our best guide, little attention has been paid, though we can make a very good guess as to its general nature. There have been identified ammonia, methylamines, ethylamines, hydrogen bisulphide, ammonium sulphide, carbon dioxide, and methane. In sewer air " alkaloidal substances " also are said to be present. Remaining behind in the sewage, in combination with alkaline bases and amines, are the volatile organic acids. When a soil is choked with organic matter, nitrification (oxidation) becomes impossible, and therefore a greater proportion of nitrogen, in the form of ammonia and fatty amines, must pass into the air.

From this evidence it is an easy transition to that indicating the potency of bacterial products emanating from the soil, and maybe also those present in the drinking-water, yet not formed by the decomposition of sewage or manure.

Haviland, as the result of an extensive inquiry, found that the incidence is higher in damp, low-lying districts, through which run streams liable to seasonal flooding, and coming from soft or marshy districts or districts containing easily disintegrated rocks, so that the water is generally highly coloured with alluvial matter. On elevated lands, well drained, and not subject to flooding, the incidence of cancer is lower. The Registrar-General's decennial reports (England and Wales) show a high death-rate from cancer in the Fen district. Cancer is also said to be common where there is water in the form of a river, lake, or marsh, and a high death-rate has been associated with defective drainage of the soil and sub-soil.

Haviland also found that persons living upon a clay soil were more open to the attack of cancer, and in this he is corroborated by Butlin and others. Amongst other facts he points out that the Thames cancer field is almost co-extensive with the London clay. The incidence was found to be lower upon sandy soils, and especially upon the carboniferous limestone. Golb discovered the highest mortality from cancer in South Germany upon a stretch of territory almost exactly corresponding with the tertiary formation, with alluvial deposits, and marked by peaty and swampy spots and extensive clay soils.

In ground air have been identified methylamine and ammonia, along with hydrogen bisulphide and carbon dioxide. and unspecified organic matters are mentioned. Of course, this must be far from being a complete account of the substances present, and other fatty amines are probably present in a volatile form, for, while methylamine is the only gaseous fatty amine, many of the simpler amines have a lower boiling-point than water, and will therefore volatilise more readily. Soil bacteria are capable of forming ammonia from certain fatty, and even aromatic, amines, and fatty amines are always changed to ammonia before oxidation takes place—the oxidation which results in the formation of nitrates to serve as plant food. In wet and clay soils little nitrification (oxidation) goes on, and we may therefore expect an increased liberation of ammonia and amines. In soils choked with water, nitrification cannot readily take place for want of the excluded oxygen, and the close texture of a clay soil does not allow easy percolation of oxygen, while its tendency to retain water acts in the same direction. Further, the reaction of wet and clay soils is acid, and nitrification is retarded for that reason also, so that neutralisation with lime is necessary to fit these soils for agricultural purposes. By experimental methods it has been found that when a soil is kept moistened, ammonia and volatile nitrogenous compounds are evolved. These substances are also evolved from a clay soil under normal conditions, and, if it is kept moistened, the emanation of volatile nitrogenous compounds is greater than when it is dry. As nitrification takes place readily upon sandy and calcareous soils because of their porosity, the lower incidence of cancer on sandy soils and on the carboniferous limestone may be given as a reason why ammonia and the volatile nitrogenous compounds (including fatty amines) should be suspected as potent agents in the causation of cancer. Of course, the most pronounced acidity is found in the soil of marshes and other collections of stagnant water. In marsh air is a considerable proportion of carbon dioxide, in addition to methane and phosphuretted hydrogen.

The peculiar odour of clay soil has been remarked upon. I have found a reference to "the poisons of unknown nature evolved by damp and filthy soils." Assertion is made that sewer air, the exhalations and emanations from human beings, and the emanations from clay soils and manure heaps give the same reaction, but I am unable to learn what this statement involves. I can understand their giving an alkaline reaction.

Flooding of the soil by the overflow of streams has more than one effect. The water drives out of the soil ammonia and nitrogenous compounds in a volatile form which would otherwise become oxidised; for a period the wetness of the soil is above the normal; and the water deposits organic matter in the soil which undergoes decay. After a shower of rain volatile substances with a characteristic odour, taken as a whole, pass into the air, but it is beyond me to determine whether they have only been driven out of the soil by the rain, or have also been evolved because a wet soil does not permit nitrification. They have been made the subject of research, but the results, as a whole, are chaotic. A result of one research is that they are volatile nitrogenous compounds.

If reference be made to the incidence in "all occupied males," it will be noted that the cancer frequency is greater among those living in London than among those living in the industrial districts, and is lowest among residents in the agricultural districts. This ought to dispose of the contention that the death-rate from cancer is high in London entirely because of the concentration of cancer cases in the hospitals. As regards purity of the air, the order of the three districts will be the same, but while this comparison is sufficiently valid in the case of the industrial and agricultural districts, there is a difficulty as regards London in that it lies in the Thames cancer field, another but not exclusive factor. French statistics show that the incidence in the towns is directly proportional to their size.

Town air contains the products of the combustion of coal and the emanations from stables, drains, and all manner of filth lurking on and within the soil. The exhalations and emanations from human beings can only pollute the air to an exceedingly limited extent. When in sufficient concentration they have a fœtid odour, and consist of ammonia and other nitrogenous substances, some of which are "alkaloidal," in addition, of course, to the predominant carbon dioxide.

It is manifest that free circulation of the air will ensure the dilution of obnoxious gases, and that stagnation of the air will allow their accumulation. Lloyd Jones found that in Cambridge most cases of cancer occurred among houses hemmed in by trees, in well-wooded parts of the town, and where houses were surrounded by high walls and were without proper ventilation. And while the increased incidence in older houses (noted by more than one observer) is presumably due to soaking of the soil and of the houses with accumulated filth, the incidence may be added to by stagnation of the obnoxious air in the close rooms, narrow streets, and small courts characteristic of the older quarters of towns. This comparatively incarcerated air has an unpleasant odour, and contains organic nitrogenous compounds along with carbon dioxide. Statistics show that in France the incidence is high among labourers in woods, and among excise officers who, in certain parts of the country, spend most of their time in isolated paths through woods. The stagnant air of woods must contain more than a normal amount of ammonia and amines, for nitrification does not take place freely in their soils. Finally, it has been found that, taking extensive areas into account, the incidence is higher in well-wooded districts and is lower in the wind-swept. The higher incidence in Herefordshire has been ascribed to the abundance of orchards.

Where general statements are made to the effect that the incidence is increased near to sewage farms and manure heaps, in damp and periodically-flooded districts, and on clay soils, details of the sources of the water-supply are not given, and we cannot therefore determine whether or not under these conditions the drinking-water plays a part. But we are entitled to assume that to some extent the water-supply is drawn from the immediate neighbourhood, and therefore contains some characteristic substances washed out of the soil.

Law Webb reported an unusual number of deaths from cancer —nine in 15 years—in a group of 20 cottages, the water-supply of which was obtained from a certain pump close to a very filthy hovel. Three of the cases were in a cottage pre-eminent for dirt and discomfort. In the case of a "cancer-house" situated elsewhere, the water-supply was got from a pump near to some old cottages and not far from a cesspool. In yet another, in which occurred three cases in one family, the water was obtained from a pump just a few yards away from a cesspool.

Armaudet, in a village in Normandy with a death-rate from cancer four times that of Paris, noted that the malady developed along a line corresponding to the districts supplied with water from certain ponds.

The endemic occurrence of cancer of the thyroid is recorded by Pick in brook-trout hatcheries in Germany. It appeared among fish confined in certain tanks or pools, and the agent was apparently in the water.

The variety and complexity of the organic matters ordinarily contained in water are said to defy analysis, and, as a rule, general statements only are made of their nature. Some are nitrogenous and volatile, and presumably are fatty amines, and ammonia is almost always present, yet the substances used for its detection also react with nitrogenous bases. I suppose that we shall have to form a general idea of the compounds present from our knowledge of the processes of organic decomposition. Less offensive than water which is undoubtedly polluted with sewage, there are waters, evidently containing different predominant compounds, which receive the respective descriptions of earthy, musty, mouldy, and marshy.

Bearing upon the points already raised in this chapter is some confirmatory evidence which, as it will be seen, could not be cited before without introducing confusion.

Basing his observations upon more than 400 cases occurring in the Leamington district, Mason adduced evidence which showed that emanations from sewage increase the incidence, though this evidence is used to enforce the parasitic hypothesis. Of his cases 67 were in houses, older than 30 years, which were built when less care was taken in the construction of drains. Beneath old "cancer-houses" ran drains which were made up of one brick laid flat, two placed edgeways, with a slate for the top. Consecutive houses in the same street were often "cancer-houses," and as many were built at the same time, and had a common drain, the sub-soil was perhaps contaminated with sewage. A large percentage of "cancer-houses" were end houses of rows, corner houses of streets, or houses on either side of court entrances, places where any defect in a drain would result in the most severe contamination by sewage. Many "cancer-houses" had also old, disused cesspools, old contaminated wells, or decayed brick sewers lying forgotten in the soil below. Those houses were the worst which were built on a porous soil, for then the noxious compounds could more readily escape. On a clay soil the incidence was less. If Mason is correct in this generalisation, it is to be noted that a different principle is involved to that based by myself upon the work of Haviland. In the one case it is a matter merely of porosity of the soil, in the other of the characteristic bacterial and chemical processes taking place in it. Mason noted that some of the "cancer-houses" had cellars. Now, a cellar is usually more or less damp, and moulds and bacteria are encouraged, and cellar air, laden with gaseous and volatile substances formed by their action, reinforced by emanations from the soil, percolates through the house above, a condition which is appreciated and provided against in Germany. It was suggested by Mason that people over 40 are more subject to cancer because they are more confined to the house, and that women are more subject than men for the same reason.

D'Arcy Power reported upon the condition of two cancerous villages. One, built on flat ground composed of gravel soil lying above the boulder clay, was well watered, and in the neighbourhood were several fens and much marshy land. The other, built on ironstone and sandstone, was divided into two parts by what was little more than a brook, sluggishly flowing. This was dammed up, and into the lake thereby formed the village drains emptied, except one which had proved such a nuisance that it was made to empty below the dam. Every two or three years the lake flooded the surrounding meadows. Fish could not live in it. The country surrounding the village was well wooded. The village itself was in a highly insanitary condition, there being hardly any attempt at drainage, and the existing drains were so ill cared for that liquid sewage oozed through the soil at one or two places and trickled over the road. Water was obtained from surface wells which were greatly polluted. Most of the villagers kept pigs. Diphtheritic sore throats, recurrent bad colds, poisoned wounds, and boils were of frequent occurrence. During the period 1869–1902 there were 15 deaths from cancer, and, had the death-rate in the village from cancer been the same as that throughout England and Wales during the period 1890–1901, there would only have been one death in 17 years. But it is necessary to note that, owing to emigration of the able-bodied to neighbouring districts, the deaths from all causes were largely those of children and old people, with a few weaklings of youth and middle age.

Dealing with another district, Power pointed out that cancer cases occurred most frequently near to the rivers. One river arose in a fen and ran a sluggish course, flowing first among marshes and then through a wooded country. A second sluggish stream also arose in a fen and traversed a marshy and well-wooded country. The whole district was flat, and showed the characteristics of marsh land ; it was well watered, and there were many streams and several fens ; and a gravel soil overlay the boulder clay. Yet it was not a very markedly cancerous district.

Some interesting facts are recorded by Behla concerning the German town of Luckau, though he used them to buttress up the parasitic hypothesis. Cancer was common in one suburb which was built upon what was once marshy land. In the other, built upon a sandy substratum, it did not occur during the 23 years under review. The soil of the first-mentioned suburb was flat, low-lying, and moist, and closely encircling this suburb and the central part of the town was a ditch containing foul, stagnant water. Most of the cases were found along the course of this ditch, especially in the suburb, the gardens of which were watered from the ditch.

Behla also has it that cancerous localities are usually found in regions richly-wooded, with numerous streams and rivers, and where there is a clay soil. The houses are frequently damp.

As the result of an inquiry made in the Fontainebleau district, Foucault asserted that nearly all the multicancerous houses ("cancer-houses") were badly ventilated, and had generally little exposure to the sun, and dampness was kept up, not only by the building materials, but also by the bad drainage for slop and rain water. He noted that the cancer mortality increased in proportion to the lowness of the site and its humidity.

It is claimed by Noel that cancerous districts are closely populated, or a stream connects them if they are spread about or at a distance from one another. I would point out that the latter probably depends upon the usual excess of ground-water near to a stream. He noticed the effect of want of slope, making for inefficient drainage of the sub-soil, in increasing the incidence.

An unusual number of cases treated by Dunn came from a riverside street in Hammersmith which was flooded by the Thames at high autumn tides. Alderson found that all of his uterine and mammary cases in the same district lived near to the river just above sea-level. One patient had lived in a periodically-flooded street for 70 years. In these cases a number of factors are probable: emanations from the polluted Thames; decomposition of organic matter carried on to the soil by the flood water; mould encouraged in the houses; the retardation of nitrification in the soil by the periodical wetness due to the floods and the permanent wetness due to excessive ground-water percolating from the river; and driving out of unoxidised nitrogenous compounds by the incoming water, the latter a very slight factor.

As reported by Ackerley, a "cancer-house" at Surbiton was built upon low ground 20 yards from a stream, and possessed cellars which were below its level.

Haviland found that a certain "cancer-house" was situated in a hollow, with a clay soil, cradled by ridges rising to 500 and 600 feet within a radius of half a mile. The upper part of the hollow was relatively dry, but the lower was damp, and alders, rushes, and mosses grew luxuriantly, everything being apparently sodden. The house stood 20 feet above the level of a stream, which sometimes flooded its banks.

A Committee was appointed by the Birmingham and Midland Counties Branch of the British Medical Association to collect evidence of the distributional and other details of cancer cases. Extracts from the report of the Committee are given below. The report was compiled in 1899, and, for the purpose of comparison, I may mention that the average mortality from malignant disease in England and Wales was 0·58 per cent during the period 1889–90. The returns extend, with one or two exceptions, over a period of ten years.

The M—— registration area had a cancer death-rate much above the average. This was chiefly due to the high incidence in a group of parishes: M——, 1·77; H——, 1·74; G.P.——, 1·3; and L.P——, 1·98. The rates were 0·68 and 0·51 respectively in the adjoining parish of C—— and in C—— itself. In the opposite direction there was a decrease. until there was reached F—h—l, 0·34. Wall reported of the M—— registration area, especially the sub-district of H——, that some parts of it were very marshy and low-lying. C—— was on the steep slope of a hill, and the F—h—l district was on higher and drier ground.

The T——h district was reported upon by Rubra. Nearly one-third of the deaths in the township of T——h occurred in a small area a little more than a quarter of a mile in length, the death-rate (1·9) being nearly four times that of the rest of the district. The river Tame, a sluggish black stream, highly polluted with sewage from the Birmingham district, flowed in close proximity, and some of the houses were on its banks. As a boring, made a little further from the river, showed that the ground-water rose to the level of the stream, the polluted river-water probably percolated through this area. The sub-soil—mostly clay and gravel—was very damp; ground fogs were prevalent; and floods were not unknown. Most of the inhabitants of this area were poor people living in mouldy old cottages, the floors and walls of which were generally damp. The water supply came from deep wells two miles away, and was excellent.

Fifty cases occurring in B—— were investigated by Martin. A group of "cancer-houses" were close together in two adjacent streets. Built on clay, they were some of the oldest houses in B——. Opposite them was a big ditch, which nearly always contained water, and behind this was the churchyard, on a level two or three feet above them. In the case of one of the streets, the houses were very damp, and always had water in their cellars. He made this general statement: "The 'cancer-houses' occur in groups; nearly all are built on clay; all but one are damp. Part of B—— is built on sandy soil, and, although the houses here are very dirty and the inmates poor, they are almost free from cancer."

Martin commented upon W—— as follows: "The town is built partly on a sand bed, partly on a clay bed of varying thickness, overlying a bed of limestone. This clay bed has in many cases been thrown out into mounds to get at the limestone. Houses have been built upon these clay banks, and, speaking generally, these are the houses where cancer occurs. They were all damp, some very much so. They were among the oldest houses in W——. The new houses are almost entirely free. Parts of the town built on sand beds are free, although in most of these positions the poorest of the inhabitants live crowded together under anything but sanitary conditions. The sand and clay beds are in places sharply defined, a 'cancer area' on the clay bed being likewise sharply defined from an area almost free from cancer contiguous to it on a sand bed."

Rowland reported upon the L—— district. The highest rates were in E—— (1·87), Ch—— (1·5), and C—— (1·52). The two former were very low-lying, practically upon the water, and were subject to floods. The small village of C—— was on a hill high above the sea-level, but a stream ran through it which, though rapid, fell under suspicion of pollution two years before. The cancer death-rate in the neighbouring district of R—— was 0·71, in the town of R—— 0·77, and in the town of A—— 0·79. The latter lay between the rivers Trent and Tame, and was very flat and low. Water could be reached anywhere at from four to five feet down, and the soil was black, sandy peat. The town of R—— was low-lying, and was skirted upon one side by the Trent, and the meadows close to the river were generally flooded after a heavy rain. The soil was a loose gravel, with the line of saturation from 12 to 14 feet below the surface.

From Murray's report upon the T——y union may be given the following extract: "The parishes which have the highest rate of mortality for malignant diseases are, with one exception, those which lie in the Tame valley and on the south bank. The sub-soil, I believe, is gravel. The river receives untreated the sewage of L—— and T——, and all the valley is very liable to ground fogs almost nightly. The parishes which are free as a rule lie on higher ground."

This committee was appointed after the reading of a paper by Nason, whose conclusions are sustained above.

I would here point out that the putative causes of goitre resemble, as a whole, those agencies which we have been considering in this chapter. Credit has been given to dampness in houses and the want of fresh air in them; and to cellar-dwellings, ill-ventilated schoolrooms, and houses in damp, ill-ventilated streets and courts. The incidence of goitre is higher upon low-lying marshy ground in valleys, where the emanations from the wet ground will lurk in the relatively stagnant air. It is also higher where large rivers often break their boundaries. The causative agent is sometimes present in water, and is destroyed by boiling. Water from calcareous strata has been blamed, which is a source of difficulty to me, though I may recall the assertion that when chalk is moistened an odour is given off like that emitted by the ground after a shower of rain. I am somewhat suspicious of "the clear, sparkling water with an agreeable taste," containing much carbon dioxide, got from the chalk. In this connection some importance may be attached to the recent work of Hall and Miller upon nitrogenous compounds present in soils and evidently derived from humus deposited in the parent rock while the latter was being formed.

Epidemics of goitre in schools, barracks, and other institutions may be due to the sudden onset of the potent substances.

CHAPTER V.

THE LIQUOR TRADES. ALCOHOLISM.

Brewer [*Cancer*—81 (51), 112 (63) ; *Alcoholism*—48 (15), 46 (16)]. *Inn, Hotel—Servant* [*Cancer*—75 (51), 88 (63) ; *Alcoholism*—112 (15), 105 (16)]. *Maltster* [*Cancer*—69 (51), 60 (63) ; *Alcoholism*—17 (15), 12 (16)]. *Innkeeper, Publican ; Spirit, Wine, Beer—Dealer* [*Cancer*—61 (51), 66 (63) ; *Alcoholism*—106 (15), 129 (16)].

I CAN best begin by describing the processes of manufacture of the two principal alcoholic liquors—beer and whisky. The less popular liquors will be ignored.

The first stage in the manufacture of beer is the production of the malt. Barley is allowed to germinate to a slight degree—when carbon dioxide is liberated and is carried away by more or less perfect methods of ventilation—and it is then subjected to the action of heat (kilning) for certain reasons : (1) to stop the germination ; (2) to cause the formation by roasting of substances which impart to beer part of its characteristic aroma and flavour ; and (3), as concerns almost all beer manufactured in the British Isles, to allow the barley to absorb products of the combustion of coke or anthracite which add to the aroma and flavour. The temperature to which the roasting is carried depends upon the kind of malt—pale or dark-coloured—which is required.

According to the British method of kilning, the hot fumes from fires of coke or anthracite (containing, of course, tarry matters) are allowed to pass through germinated barley spread upon perforated floors. The fumes impart a darker colour to the malt, and one lecturer on brewing remarks that they give " a pleasant empyreumatic flavour peculiar to good malt," while another notes that this flavour is retained in the beer. As it is also put : " The result has a peculiar, agreeable flavour, probably from a small portion of empyreumatic oil, which imparts its flavour to the beer." Malt prepared in this way is stored for at least six weeks before being used in order to lose the " fire," and to become mellow, but if it is stored too long it loses some of its aroma and flavour, and there is at least one patented method for treating this exhausted malt with the products of combustion of anthracite to restore these qualities. Before storing, it is said to be brushed or screened for the purpose of removing arsenic deposited from the fumes, but to what extent this is carried out I cannot learn.

In the Continental method, introduced here not long before 1890, and used only in the production of lager beer, the hot fumes from the fire pass through flues or pipes below the kiln floors, so that the fumes do not come into contact with the germinated barley.

In the third method, not very freely used in this country, the barley is heated in revolving cylinders to temperatures of between 200° and 250° C. This method is employed for the production of dark-coloured (patent) malts to be mixed with paler malts prepared by the other method. This malt must be used on the day after its preparation or the essential aroma is lost.

Where the oldest (British) method (which concerns us most) is employed, the maltster experiences some fumes from the fuel and the roasted outer part of the barley—the inner part is practically unaltered—when he enters the kiln to turn over the partly-prepared malt ; and when it is being removed from the kiln, and also when it is cooling upon the floors, there are emanations from the finished malt. Where malt is prepared in revolving cylinders, leakage of volatile substances occurs during the roasting, and there are considerable emanations while the cylinders are being discharged, which are less in degree when the malt is spread upon the floors to cool. A penetrating odour like that of burnt bread pervades the roasting-house, and tarry matter condenses upon the windows.

In the outer part of the malt-grains must be tarry products formed by their roasting and absorbed, in the British method, from the fumes of the coke or anthracite. The former will resemble more the products of coal than those of wood, for it is a highly nitrogenous part of the barley which is attacked. I have been unable to find an analysis of malt, or malt extract, which indicates the presence of any products of combustion except ammonia, and it is not to be expected that brewing chemists will dwell upon this point. Nitrogenous bases are present, but there is no indication that any are heat decomposition products, and yet the tonic properties of malt extract lead us to expect their presence. It is worth noting here that an apparatus has been devised—for commercial purposes, I take it—to intercept the volatile substances which are formed during the roasting of coffee. Some of these substances have been identified : caffeine, methylamine, trimethylamine, pyrrol, furfural, and acetic acid. Roasted coffee beans are sometimes glazed in order to prevent the loss of "alkaline vapours." Glucosamine is present in malt, but I am uncertain of the value of this observation.

The hot-water infusion of the malt—the wort—is boiled with the hops added. In the year 1890 heating the wort by steam, now the general method, was only coming into vogue. The earlier method, with which we are concerned, was that of allowing the fire to play upon the copper, when there was some decomposition of solid particles in the wort. From the hops are extracted during the boiling an essential oil (a hydrocarbon) which gives an aroma to the beer, tannic acid, and various substances of a bitter nature (two hop-bitter acids in combination, choline, alkaloidal substances, including hopein and lupulin, and a non-nitrogenous substance with the properties of an aldehyde and a weak acid). Hops are dried by the fumes from fires upon which is sometimes sprinkled sulphur, not always free from arsenic, in order to bleach the hops, to give them an added flavour, and to kill mildew.

After boiling, the wort is cooled, and yeast is then added. During fermentation are formed higher alcohols as well as ethylic, fatty acids and their esters, various ethers, and carbon dioxide. I give with all reserve the statement that hydropyridic bases are formed during the fermentation of sugar with yeast. Some of the nitrogenous substances in the wort are altered by the yeast, but I am without knowledge of the products which are formed.

The next part of the process of importance from our point of view is the fining or clearing of the beer. Isinglass or other gelatinous substances, dissolved in sour beer or sulphurous or tartaric acids, is added, when it agglutinates, and thereby are collected together all particles which make the beer turbid. Some of the isinglass substitutes are made from fish waste, but I do not expect that they are obnoxious.

Preservatives are finally added, such as the acid bisulphites of potassium and calcium, and sulphuric and salicylic acids.

The casks in which the beer is stored are coated inside with an impervious substance. In this country, before 1890, wood-pitch was used because of the aromatic flavour it imparted to the beer. Nowadays this flavour is not so much desired, and various mixtures containing resins, resin oil, linseed oil, yellow (impure) paraffin-wax, or tallow are displacing the pitch, or certain of these substances are combined with it. The latter, once used for lining the fermenting vats, is there also being displaced.

There is a secondary fermentation in the cask.

This account of the processes of brewing does not exhaust all of the possibilities of the brewer's "art." Many other substances than those above mentioned are put into beer. Invert and caramelised sugar is used, and sugar caramelised under pressure in the presence of ammonia, when a glucosine may be formed. Molasses is another raw material, and torrefied grain, that is, grain which is gelatinised. As hop substitutes, or for unscrupulous purposes, are used capsicum, guinea pepper, grains of paradise, quassia, camomile, juniper berries, horehound, wormwood, chireta, simaruba, and colombo root. Popular report has it that the publican brings his "art" to bear, but upon this point there is no very extensive evidence and prosecutions are rare.

Barley is liable to be attacked by moulds and bacteria before it reaches the brewery and during germination. Formerly, when the wort was not so quickly cooled after boiling, attacks by bacteria were looked for, and are yet expected during fermentation, though some precautions are now taken. Accumulations of material in the apparatus, due to want of cleanliness, make matters worse. Further decomposition may ensue in the cask ; of course, if it is pronounced, the beer receives a special treatment.

What is the composition of beer ? Brewing chemists tell us about the ethylic alcohol (seldom mentioning the fusel oil), carbohydrates, glycerine, volatile and fixed fatty acids and their esters, phosphates, hop extract, albuminoids, amides, and amino-acids, but we want to know also what are the heat decomposition products which are present. The probable potency of some of the above-mentioned substances will be pointed out later, but the latter products may be more potent. Arsenic is present in beer in varying quantities. I have not found any record of the presence of ethers.

As it reaches the consumer, whisky is generally so blended that it may safely be asserted that a number of kinds of material have been used in its manufacture. The most familiar are unmalted barley and other cereals, beetroot, potatoes, sugar, molasses, and malted barley. There must be little whisky upon the market into the manufacture of which malted barley has not entered in some degree. The barley is kilned upon perforated floors, and in the case of much Highland and Irish whisky peat is used as a fuel, a characteristic flavour being given to the whisky. Kiln temperatures are not so high for whisky as for beer malt. In some cases the malt is roasted in revolving cylinders.

If grain, malted or unmalted, is used, it is mashed in hot water, and to the wash is added yeast, fermentation being carried on during a longer period than in the case of beer, so that more alcohol is produced. Coming next is the process of distillation, and in this two kinds of still are used—the pot and the patent still. The pot still is practically a metal retort; and while in some distilleries stirrers are employed to prevent solid particles from settling upon the bottom of the copper, where they become burnt, in other distilleries this burning is allowed to take place in order to add to the whisky a smoky or empyreumatic flavour which is appreciated by some. In the patent still the wash is not directly heated, but is allowed to drip slowly down a series of trays in a chamber through which passes a current of steam. The steam, condensed in another chamber, contains the volatile constituents of the wash. In the case of both forms of still, part only of the distillate is used, and that of the pot still is subjected to further distillation, the parts condensible at the highest and lowest temperatures being rejected. The utilised part of the product of the pot still is stored for a period to allow for the oxidation and esterification of some of its constituents, the wood of the cask absorbing some obnoxious constituents also ; or it is first submitted to processes involving the oxidation or removal of these constituents. This purification, however, is not perfect. The product of the patent still can be used directly after manufacture.

The constituents of whisky have been determined in greater detail than those of beer, and yet fairly complete analyses are not obtainable. The following substances are probably present in all samples of whisky, and have been identified in some specimen or other : ethyl and higher alcohols (amyl, &c.), volatile fatty acids and their esters, phenolic compounds, furfural and other aldehydes, ketones, acetals, ethers, mercaptan, and pyridine and other aromatic amines. I suspect the presence of fatty amines, which have been detected in some samples of brandy. It is manifest that the greater the quantity of pot-still whisky in the blend the greater will be the content of heat decomposition products.

The only adulterants of which I can find a record are creosote and methyl alcohol. Mouldy grain, unfit for food, is sometimes used, when substances of an alkaloidal nature may be introduced into the whisky.

We have now seen that in whisky, and certainly also in beer, are present heat decomposition products, but it is also to the fermentation products that we will turn our attention in later chapters, for potency in the causation of cancer can be ascribed to them. They are decomposition products formed by organisms closely related to the bacteria.

Not only is the incidence of cancer high in occupations concerned in the manufacture and sale of alcoholic liquors, but among all occupations with a higher comparative mortality figure for cancer than 51, which was the rate for " all occupied males " during the first period, the average mortality figure for alcoholism was about 23, as compared with 15 for " all occupied males," while during the second period, among all occupations with a higher comparative mortality figure for cancer than 63, which was then the rate for " all occupied males," the average mortality figure for alcoholism was about 19, as compared with 16 for " all occupied males." Fox found that in 114 cases of cancer among males, the alimentary tract was affected in 64 per cent. of the non-abstainers, and in 34 per cent. only of the abstainers, which agrees with the oft-repeated statement that the imbibition of alcoholic liquor increases the incidence in the œsophagus and stomach. Yet Newsholme came to the conclusion that alcoholic liquors did not increase the incidence in specific organs, having only some general indirect effect, which he could not specify, in increasing the incidence.

It has been found that the death-rate from cancer is high in countries where beer is the staple drink, though it is curious that many observers lay stress upon spirit-drinking rather than beer-drinking as a factor in the causation of cancer of the mouth, tongue, throat, œsophagus, and stomach. I would here remark that the history of the cancer problem is practically a history of failure to accurately correlate cause and effect.

While we may take it that the imbibition of alcoholic liquors is causative of cancer in the liquor trades, it is probably not the only channel through which these liquors exercise their influence. That the inhalation of fumes from the liquor helps to increase the incidence is rendered probable by the evidence already cited showing the effect of living on damp and clay soils and in the neighbourhood of sewage farms and manure heaps, which we may take as proof of the potency of volatile substances. The low death-rate from alcoholism in the case of maltsters, and their comparative freedom from the attack of fumes arising from the manufactured drink, throws the responsibility for the high incidence of cancer among them upon the tarry emanations from the fires and the malt. Whether or not they, along with the brewers, suffer from cancer the more because of the carbon dioxide liberated during germination and fermentation respectively is a matter which I cannot determine.

Alcoholic liquor may not be the only agent among occupations concerned in its sale. Inn and hotel servants have sometimes to sleep in cellar bedrooms, and their sleeping accommodation is often insanitary. Along with the innkeepers and publicans, they experience the typical air of cellars, which must also be heavily laden with alcoholic fumes, and there will be percolation of this air upwards into the public rooms. All must also suffer the exhalations and emanations from the lungs, skin and clothes of customers—" crowd poison "—as well as from the effects of inhaling copious tobacco smoke.

CHAPTER VI.

Indirect and Direct Action of the Decomposition Products in the Causation of Innocent and Malignant Growths.

HAVING reviewed the evidence implicating the decomposition products, we are next confronted by the problem of their mode of action. Have they a direct causative action, or do they first induce a precancerous, inflammatory condition? My suggestion is that both of these questions may be answered in the affirmative. The decomposition products, coming into contact with skin or mucous membrane—in the case of the latter the volatile products are included—play a part in inducing or aggravating an inflammatory condition, and, acting further along with inflammatory products, they upset locally the control which is exercised, in some unknown way, upon the growth of the constituent tissues of the body. (The inflammatory products referred to are bacterial and autolytic decomposition products, though they are of a somewhat different nature, taken as a whole, when compared with the bacterial products formed outside of the body, the most marked difference probably consisting in the greater proportion of albumoses and peptones and more complex products, which will exercise some effect before they are again decomposed.) Further, the decomposition products can act directly, in upsetting the control of tissue growth, without interposition of an inflammatory condition. Constantly inhaled, and passing into the blood, the volatile decomposition products will induce or aggravate inflammatory conditions and exercise a direct effect.

In due course I will recite evidence implicating inflammatory conditions as precursors of cancer, and, it may be said, of innocent growths; and evidence will also be recited of the causation, or aggravation, of inflammatory conditions by the decomposition products. I will also show that some decomposition products, by direct action, cause the formation of certain kinds of innocent growths, warts particularly, and the same will be shown for inflammatory products and decaying secretions. As concerns the direct causation of cancer by decomposition products: We know that contact of soot with the skin sometimes leads to the formation of warts, and that they may become cancerous owing to continued action by the soot, or as a result of mechanical irritation.

That they become cancerous in some cases as a result of mechanical irritation points towards the conclusion that, when they become cancerous by the continued action of soot, it is because the soot has then an irritative, inflammatory action. Yet there is no doubt whatever that decomposition products are direct causes of cancer, and in the example just cited it is even possible to ascribe potency to direct, non-inflammatory action by the soot and mechanical irritation. As far as the causation of cancer by inflammatory products is concerned, its inception in an inflammatory lesion is not, of course, sufficient proof, and we ought to have evidence showing that it has developed in a previously healthy tissue, away from the site of the inflammatory lesion, but bathed by its discharge, and that without the interposition of further inflammation in the site of the cancerous growth. Some doubtful evidence upon this point will be cited in the next chapter.

In spite of uncertainty in the evidence, the succeeding part of this book is based upon the hypothesis that both decomposition and inflammatory products—terms which are not perfect, but yet are convenient—are direct agents in the causation of cancer.

The evidence showing that the decomposition products directly induce the formation of certain kinds of innocent growth will now be repeated. That it should be so strong in the case of warts is important, for cancer begins frequently as a warty growth, while warts are liable to appear among the members of cancerous families. That they occur most frequently upon the hands encourages us to believe that decomposition products are concerned in their causation.

Warts are common upon the bodies of sweeps—Paget saw some hundred or more in one case—especially on parts which come the most into contact with the soot. Soot merchants may have warty hands, and gardeners also who spread soot in the course of their occupation. A general thickening of the skin may follow its repeated application. Men employed in mineral oil works and coal-tar distilleries, and those who deal with liquefied pitch, are also liable to warts. Butlin was informed by an oil worker that his mates kept their skins clean to avoid warts as well as sores. Those employed in the isolation of anthracene from coal-tar are especially prone to be warty, and Butlin recorded that an anthracene worker had his trousers habitually soaked, so that warts existed below. Crude anthracene contains basic impurities (nitrogenous, such as acridine) removable with sulphuric acid, while in one process of purification, pyridine, aniline, and quinoline bases are used also, presumably to extract acids. Distillers of benzene—commercial benzene contains pyridine bases—and creosote are said to be less liable to warts than the anthracene workers. Oliver found numerous warts upon the hands and forearms of men employed in mineral (waggon) grease works, and if warts were present when the employment was first begun, they disappeared; but according to a later statement the warts developing after employment began exhibited the characters of true epithelioma, while it is also asserted that warts already on the hands when work in tar and creosote is commenced are often lost, but recur later. The papillomata of the bladder in workers among aniline, &c., may be recalled. Warts occur on the bodies of those employed in carbolic acid manufacture, even those who handle the purified product. It may be that inhalation of the vapour is partly responsible.

Hebra mentions the belief of the older physicians, held also by the general public, that warts are common among those associating with the lower animals and coming into contact with them. I have found a statement to the effect that they are common upon the hands of agricultural labourers, whose hands, of course, must frequently be polluted with manure and damp soil. Another assertion is that they occur upon the hands of those performing manual labour. Warts are found upon the muzzles of lambs allowed to grub in farmyards and in the muddy, stagnant farmyard ponds, into which frequently drain the washings of manure heaps, stables, and byres. Among the compounds identified in soils, in addition to fatty amines and humins, is picoline-carboxylic acid, picoline being one of the pyridine series.

They are found upon the hands of boys who do not wash often enough, and they are then curable sometimes by cleanliness. Repeated dirtying and moistening of the hands is said also to be responsible, while the wearing of gloves involves a lessened liability. Humphrey found that warts were most numerous among persons employed in dirty work—sweeps, servant lads, and scullery maids. Warty scars are said to be due to uncleanliness.

Decomposition products absorbed into the blood from the intestine appear to be agents. As a cure for warts Colrat recommended the administration of magnesium sulphate so as to produce at least three evacuations a day. This treatment answered in some cases. Chalmers Watson treated with castor oil a case of numerous warts, there being a history of constipation lasting for a year, and a cure resulted. Crocker used magnesia in small, oft-repeated doses sufficient to produce an aperient action. A case with a history of constipation was cured by Hall upon administration of pills of aloin and nux vomica. In other cases he gave mistura alba three times a day.

Jamieson has, in some cases of digitate warts of the scalp, traced their origin to the use of rancid hair-oil or pomade. Lard and beef marrow enter into the composition of pomades, while olive oil probably contains characteristic products. Nitrobenzene appears in some hair oils, while mineral oils may be suspected as adulterants.

The warty growths upon the knuckles of butchers and knackers are tubercular, and this is the case with some, if not all, post-mortem warts, though the statements are persistent that these are due to the action of acrid fluids of the cadaver. Warts upon the hands of women engaged in cooking and washing are also said to be tubercular. An inoculable form of wart appears upon the udders of cows and upon the hands of milkers. These facts demand that some of the statements previously made should be treated with reservation.

Scanty evidence is to be obtained in the case of other forms of innocent growth. Drinking of alcoholic, especially malt, liquors predisposes to diffuse and circumscribed (multiple) lipomatosis, but I am not certain that any tumour formation takes place. The so-called "lipoma nasi," which is a fibrous growth with enlarged sebaceous glands, appears in alcoholics and dyspeptics, and in the latter putrefaction in the stomach is to be expected. Exposure to the weather is probably an additional (superadded) cause. In face of the suggestion that reflex irritation of the facial nerve is responsible for the development of rhinophyma, I was in doubt at first about the validity of mentioning it here. Later this point will receive notice. I have found some slender evidence showing that molluscum fibrosum (neurofibromatosis) and hypertrophy of the gums may appear under bad hygienic conditions.

While condylomata are in most cases venereal in origin, uncleanly habits undoubtedly play a part in their causation.

I have given extended consideration to the question of the direct causation of cancer by decomposition products. It is very treacherous ground upon which to tread, for the complete history from an histological point of view of cancerous growths, not preceded by inflammation, is seldom obtainable, particularly of any due to the action of decomposition products. One of the most typical examples is the epitheliomatous wart reported by Oliver in mineral grease workers. As in the case of ordinary warts, antecedent inflammation is not recorded. When the action of certain other forms of agent than the decomposition products comes to be considered, we will find how often antecedent inflammation in the site of the growth fails to be recorded. And the appearance of extensive multiple sarcoma of the skin can only be ascribed to the direct action of a toxæmic condition.

CHAPTER VII.

THE CAUSATION OF INNOCENT AND MALIGNANT GROWTHS BY INFLAMMATORY PRODUCTS.

IN the last chapter I showed the causative relationship between decomposition products and warts, and, as it is part of my case that the products formed in the seats of inflammation act like decomposition products, evidence will now be led of the causation of warts, papillomata (which are warts of the mucous membranes), and other excrescences by inflammatory and other abnormal discharges and by decaying secretions. The objection may be made that I am stretching a point in including the latter, but, on consideration, their homologous nature will be recognised.

Discharges from chronic ulcers of the mucous membranes may lead to the formation in their neighbourhood of papillomata and polypi, or merely to a condition of diffuse hypertrophy. Around the anus are sometimes found excrescences, frequently pedunculated, the result of irritating discharges from the bowels, being common in stricture and chronic ulcer of the rectum. On the lips of and around the urethral orifice may occur small papillomatous or cauliflower warts, due to irritating discharges arising in the urethra or kidney, and warts are sometimes found about the orifices of urinary fistulæ. Caused by irritating discharges from the vagina in pregnant women who are not too cleanly, warts may appear upon the vulvæ and in the perineal region. In men, horses, and bulls warts are found upon the glans and prepuce in cases of phimosis, and are due to the action of decaying smegma. At least three observers record warts on the index and middle fingers of young females addicted to onanism, and Kretschauer found them upon the index finger of a girl who was accustomed to insert this finger into the cloaca of hens to determine the near-laying of eggs.

In the case of warts about the orifices of urinary fistulæ, and those present in phimosis, decomposing urine may also operate.

The most important point about this evidence is that, except in the case of warts due to decaying smegma, the excrescences arise away from the place of origin of the products, so that it must therefore be admitted that excrescences forming in the seats of inflammation are also caused by what I have, for convenience sake, called inflammatory products.

Our next step is to inquire what is the evidence that inflammatory and other abnormal discharges induce malignant growth in parts that are previously healthy ; and, of course, to be of any value, it must be shown, in some if not all cases, that these discharges do not first cause the formation of a precancerous, inflammatory condition. In this respect the evidence is not satisfactory, and it is impossible to pronounce an opinion upon this point. In at least one case the discharge produced a precancerous, inflammatory condition.

Cancer is reported at the openings of sinuses where tubercular bones discharge their pus, and at the margins of issues, where a foreign body is used to maintain the opening. Paget recorded a case where a man suffering from stricture of the urethra had numerous urinary fistulæ in his scrotum and perinæum, cancer developing about the orifice of one of the openings. I have unearthed a general statement to the effect that malignancy supervenes on surfaces irritated by the discharges from mucous membranes, by glandular secretions, or by discharges from chronic eczema, but the basis of fact is not given. Another general statement is that cancer of the vagina has been ascribed to discharges from the uterus, but to this it is a valid objection that cancer of the vagina should therefore occur more frequently.

Discharges from cancerous growths seem to be potent, and they are comparable with other irritants of bodily origin. Petersen described a case of cancer of the uterus in which the vulvæ and the skin in their neighbourhood became red and eczematous, small cancerous nodules and ulcers appearing later. Innocent growths, such as adenomata, have also been ascribed to cancerous discharges. But the most important evidence is afforded by the process of autoinoculation. This phenomenon is one of the main buttresses of the parasitic hypothesis, yet it can be given another explanation. In every case of autoinoculation into which I have looked, ulceration has begun in the primary growth before the apposing surface showed any signs of abnormality. My suggestion is that the cancerous (ulcerous) discharge induced the formation of the secondary growth. There will at once be called to mind those cases in which epithelioma develops at the edge of a chronic ulcer, possibly because the ulcerous discharge bathes the bordering tissues.

Petersen's case is the clearest of this evidence, and we know that inflammatory discharges are capable of producing further inflammation in the neighbourhood of orifices through which they flow. But the state of affairs in cases of autoinoculation should enable us to determine the point at issue, and perhaps Butlin will be good enough to express an opinion upon this point. Some of the cases recorded by him suggest direct, non-inflammatory action on the part of the cancerous discharge.

Our present position may be summed up as follows : It has been shown that some forms of innocent growth are directly induced by the decomposition products, and that growths of a similar character owe their origin to inflammatory and other abnormal bodily products ; positive proof of the direct causation of cancer by the latter has not been adduced, while there is some evidence in the case of the decomposition products.

It is my intention now to show that the decomposition products are agents in inducing or aggravating inflammation, and in order to fully justify this course I will in the next chapter produce evidence that malignant and innocent neoplasms develop within inflammatory lesions.

Attention should be drawn, before proceeding further, to the granulomata and other forms of hypertrophy resulting from the presence of parasites in the tissues, and manifesting themselves in tuberculosis (including the tubercular warts of butchers, &c.), syphilis, leprosy, molluscum contagiosum, actinomycosis, mycosis fungoides, frambœsia, madura, yaws, rhinoscleroma, and verruga peruana. May we add to these the supervention of warty conditions upon condylomata and in the lesions of lupus ? Certain granulomata have a strong resemblance to sarcoma. Actinomycotic tumours were once described as sarcomata, and it is a striking example of the effects of parasites upon the tissues that some tumours which would clinically be described as sarcoma are examples of yeast infection. Another important example is the infective sarcoma of dogs. We are without knowledge of the nature of the excretory (?) substances to which the abnormal growth is due.

CHAPTER VIII.

ABNORMAL GROWTH AS A SEQUEL TO INFLAMMATION.

VERY familiar is the inception of cancer in inflammatory conditions—generally chronic—of the mouth, tongue, throat, œsophagus, stomach, and large intestine ; of the kidney and bladder ; of the glans and prepuce (as in the case of balanitis due to phimosis), parts which are seldom affected in Jews and Mohammedans ; of the uterus and mammæ ; in fact, of practically every organ or part of the body. Eczema, psoriasis, and herpes sometimes lead to cancer, and another inflammatory affection of the skin—Paget's disease of the nipple—nearly always does so. Among the less familiar examples are : cancer of the vermiform appendix as a sequel to appendicitis ; epithelioma, sometimes multiple, in cirrhosis of the liver ; cancer in chronic inflammation of the lung ; epithelioma, sometimes multiple, upon a basis of chronic seborrhœa ; carcinoma in kraurosis vulvæ ; and cancer following suppurative otitis.

Cancer may develop in the seats of chronic ulcers of the skin, tongue, stomach, &c., especially when they are irritated ; and in the case of ulcers of the skin, also when they are neglected and dirty. It occurs most frequently in the stomach in the pyloric region, where ulcers are commonest. While most observers record a low percentage of cases of gastric cancer developing in ulcers, Rodman points out that the latest statistics give a high percentage. Moynihan records 72·1 per cent, Robson 59·3 per cent, and Mayo 60 per cent. Zenker has it that an ulcer precedes in all or almost all cases.

Cases are reported in wounds which refuse to heal, and in scars which often break out. Cancer may develop upon the lesions of lupus vulgaris, and less often, of lupus erythematosis. In many, if not all, cases of canker in horses it is preceded by chronic inflammation, especially in the form of thrush.

A very important point in the association of cancer with inflammation is the evidence showing how frequently cancer patients have a past history of syphilis. The estimates of the percentage of syphilitics among cancer patients vary from more than 80 per cent to the vanishing point. While the higher estimate is probably exceptional, with respect to the lowest estimates we must remember the amount of evasion practised. I need hardly recall the great tendency in this disease to the formation of inflammatory lesions, yet it is only in a comparatively small percentage of cases in syphilities that the malignant growth has been proved to begin in a syphilitic lesion, generally an ulcer. While the potency of syphilis may depend upon its inflammatory tendencies, in a later chapter I will mention one of the constitutional effects of syphilis which possibly is a factor in increasing the incidence. As stomatitis and glossitis sometimes result from the use of mercury and potassium iodide, we must bear in mind the possibility that their use increases the incidence in the mouth parts.

Gonorrhœa is a form of inflammation appearing to play a part in the causation of cancer, which is proved only in some cases of gonorrhœa to develop in its lesions. Though Dieffenbach, for example, reported a history of gonorrhœa in the majority of his male cases, we must look upon this, in the face of other statistics, as extreme.

The stock objection to the suggestion that syphilis and gonorrhœa are causative agents is the comparative rarity of cancer among prostitutes, but I understand that these women are, as a rule, short-lived, and therefore do not usually attain the cancer age, while the tendency for some of them to marry must reduce the proportion of older persons engaged in this life.

Just as cancer develops in mucous membranes which are the seats of inflammation, so also may papillomata and polypi. Stopping short of the formation of polypi, there may result a diffuse state of hypertrophy of the mucous membranes, affecting different layers maybe in different cases, and sometimes also including the glands. This hypertrophied condition may manifest itself in ridges or folds, or prominences which are transitions to the polypoid state. It will be unnecessary to specify the various localities in which papillomata and polypi form, but there may be recounted some examples of innocent growths forming elsewhere than in mucous membranes.

In caries, epulis may appear in the gums and polypi spring at times from the tooth-pulp. Multiple adenomata of the liver are nearly always associated with cirrhosis, and one observer, at least, reports that in most cases of adenoma of the kidney, the latter is granular. Bony growths result from chronic inflammation of the dental cement, and in the skull as a sequel of local periostitis. Chronic inflammation of the nerve-sheaths or adjacent tissues may cause the formation of neuromata. Keloid (using the term in a liberal sense) appears in lesions of eczema, impetigo, acne, herpes zoster, furunculosis, syphilis, tuberculosis, leprosy, and smallpox, and in chronic ulcers and vaccination scars. Strachan reported that in the West Indies it was the usual occurrence in the pre-antiseptic days for surgical scars to take on keloid action. Finally may be mentioned the occurrence of "grapes"—enlarged and highly-vascular papillæ—upon the feet of horses in bad cases of grease, an inflammatory trouble.

CHAPTER IX.

THE DECOMPOSITION PRODUCTS AND THEIR INFLAMMATORY EFFECTS.

OUR next step is to collect together, as far as we can, what is known of the production or aggravation of inflammation by decomposition products, including here alcoholic liquors. And it is important that we should learn what special liability to inflammatory attacks is involved in the pursuit of certain occupations previously considered, or is due to living under certain environmental conditions. Taken as a whole, we are practically without knowledge of the regional distribution in the body in the case of the respective occupations of what we may call trade cancer, so that had we complete information, which we have not, of the regional distribution of inflammatory conditions in these occupations, the one could not be co-ordinated with the other. The best course, then, is to collect together everything with a bearing upon the subject of this chapter. If the following notes are not complete, it is because the desired information is buried deeply in the literature, and the demands made by other parts of the subject make it difficult to devote more time to its unearthing.

To eczema of the scrotum chimney sweeps and workers among mineral oil are very liable; workers in tar to a less degree. It may be aggravated by friction and decomposition of sweat. Chimney sweeps complain of conjunctivitis and pharyngeal, laryngeal, and bronchial catarrh ; and from catarrh of the respiratory passages and gastro-intestinal troubles gasworkers suffer. Eruptions in the skin of the latter, which have been ascribed to the action of heat, may be due partly, if not chiefly, to irritation by decomposition products. The leakage of coal-gas in a house induces ulcerated sore throat, which is a hint to us that gaseous substances are potent in causing respiratory troubles in the case of gasworkers ; on the other hand, decomposition products in the soot operate in chimney sweeps. Workers among carbon bisulphide suffer from skin eruptions, conjunctivitis, catarrh of the respiratory passages, and inflammation of the tonsils.

Those employed in the isolation of naphtha, anthracene, &c., from tar, or in the refining of these substances, and asphalt-workers also, are liable to varied skin eruptions, one form being acne-like. Facial seborrhœa appears among tar-distillers and naphtha-workers. The employees in tar-distilleries, and in pitchworks, where vapour is given off during the pouring and solidification of the pitch, complain of conjunctivitis, irritation of the nasal mucous membranes, and bronchial catarrh; and dust formed by the pounding of pitch causes ulceration of the nose, bronchial catarrh, and digestive disorders.

With regard to the action of the separate components. We may take it, to begin with, that the acid substances are all caustic in action. Ammonia vapour is an irritant to the eyes and respiratory passages, and, in solution, induces eruptions in the skin. Aniline is an irritant, and the workers suffer from skin eruptions and ulcers of the legs ; its passage into the urine after inhalation results in irritation of the bladder among the workers, and the development even of cystitis and strangury. The vapour of toluidine has similar effects upon the bladder in these workers. Quinoline irritates the skin. The dust of acridine, in very minute quantity even, causes violent sneezing and coughing, and very dilute solutions of its salts produce a stinging sensation on the skin and tongue. Workmen suffer so much when subliming crude anthracene that they require to protect the skin of the face with fat. The cyanogen compounds appear to be irritants.

A bout of smoking may produce an inflamed condition of the throat and excoriations in the mouth and upon the tongue. Chronic erythema of the pharynx due to repeated bouts may culminate even in vesication. Tobacco smoke also irritates the nose and eyes. Smokers are said to be notoriously liable to colds in the head, bronchial catarrh, and other congestive disorders of the respiratory passages, and it is otherwise admitted that smoking induces or aggravates stomatitis, chronic superficial glossitis, and catarrhal conditions of the throat. A syphilitic lesion may be determined in the mouth and on the tongue by smoking, and the leucoplakia of the tongue—appearing mostly in syphilitics—may occur where a stream of smoke from pipe or cigar impinges upon the tongue.

As concerns the constituents of tobacco smoke, there is nothing to add except to note that nicotine is an irritant to mucous membrane.

Among soap-boilers occur laryngeal, bronchial, and gastro-intestinal catarrh, and in the old days acrolein was perhaps the worst offender against the respiratory passages. Eczema of the abdomen is reported, and is due to their carrying vessels of fat which probably contains free fatty acids. Gluemakers are predisposed to irritative conditions of the skin. The emanations from glueworks and manure-yards make diseases more severe and prolonged, and this will presumably apply to inflammatory conditions. Gases evolved during the manufacture of superphosphate are extremely irritating. Butchers and fish and game dealers are liable to an erythema of the skin caused by decomposing animal matter, and butchers alone are said to be very prone to skin eruptions, boils, and acute inflammation.

The continued decomposition of stagnant fæcal matter in the large intestine may induce local inflammatory conditions, while constipation encourages the development of some skin eruptions. Ingestion of putrid food encourages catarrh of the stomach, the poisons acting upon the mucous membrane, and ulceration may ensue. There is the same tendency when, owing to physiological defects, food which is previously harmless begins to putrefy after ingestion. Absorption of decomposition products from food predisposes to conditions of inflammation and ulceration throughout the body, and when an infusion of putrid meat is injected subcutaneously, skin eruptions are produced. It is the ptomaines in putrid food which are the principal potent agents, as experiments and clinical and other evidence would show, and the evidence implicating other compounds is very meagre. Bacterial " toxins " retard cicatrisation and delay healing of wounds, even when injected at a distance from the wound, and a similar effect is to be expected in the case of inflammatory lesions.

Chronic sore throat may be caused by the inhalation of sewer air and the emanations from manure. There is a record of erythema nodosum due to sewer-gas poisoning. A phenomenon somewhat comparable with the former is the weakening of the throat by inhalation of sewer-gas to allow attack by diphtheritic germs. Insanitary conditions, their nature not being specified, are credited with the causation and aggravation of inflammatory states of the body. Chronic catarrh of the respiratory passages in horses has been ascribed to the foul air in ships' holds and in mine stables, and also to coming into stables after a spell in the open air. Thrush, grease, and other inflammatory conditions of the feet in horses, frequently occurring in neglected stables, are induced by dung, urine, and decaying moss-litter, while thrush may also be brought on by the use of cow-dung as a stopping for soft frogs. Decaying urine, as well as smegma, is a factor in the causation of balanitis in cases of phimosis.

The emanations from damp and marshy ground and from clay soils encourage catarrh of the respiratory passages, while clay stoppings for soft frogs in horses are said to induce thrush. I would like to know what is meant by "swamp itch" and "farmer's itch." An erythema of the skin of horses—" mud fever "—is ascribed to some irritant present in soils, and we are thus prepared for the belief that volatile products from the soil can be irritant.

Of the definite compounds, other than ammonia and its salts and the fatty acids, the amines may be the most important. They are irritants to mucous membranes. When trimethylamine is injected subcutaneously, the wound inflames and ulcerates, taking a long time to heal. Given to a dog, there ensues gastric and duodenal catarrh, accompanied by ulceration.

Sickness is badly borne by brewers' workmen, and injuries are liable to produce serious results ; perhaps, then, we may expect inflammation to run a more severe course. Though they are said to be dyspeptic sometimes, and to suffer from irritative conditions of the urinary passages and bladder, so little attention has been paid to such points as we desire to determine that these observations may not represent the whole state of affairs. The fumes from malt roasted in revolving cylinders irritate the eyes and throat, and we can judge from personal experience of the irritant nature of the fumes from fires. Attendants in public-houses and waiters acquire eczema of the hands from contact with decomposing beer and wine left in glasses.

The imbibition of alcoholic liquors predisposes to eczema. Their immediate effect upon the mucous membrane of the stomach is hyperæmia, due to paralysis of the vaso-motor system, and by repeated action catarrh may be produced. Secretion is interfered with, and hence follows dyspepsia and a further train of inflammation. The morning vomit of drunkards sometimes contains clots of blood. Spirituous liquors are more potent than the malted in producing these conditions, catarrh of the throat and œsophagus, and catarrhal conditions of the mouth and tongue. Alcoholic liquors, through the channel of the blood, induce inflammation in the pancreas and other organs, the changes in the liver culminating in cirrhosis being the most familiar, while facial seborrhœa is found in spirit-drinkers. Wounds heal more slowly in alcoholics, and suppuration is encouraged, while inflammation runs a more severe course.

Along with smoking, spirit-drinking determines syphilitic lesions in the mouth parts. The drinking of porter is said to encourage the formation of biliary and urinary calculi, which are known to provoke inflammation sometimes culminating in cancer.

Among the components of alcoholic liquors, ethyl alcohol is a familiar rubefacient, yet the higher alcohols are more powerful. The essential oil of hops has been found to have an irritant action upon the throat, and furfural resembles other aldehydes in being a strong irritant. The heat decomposition products, taken as a whole, may be in sufficient quantity to have an appreciable effect, but of course we are without data upon which to base a decision.

Bronchitis is one of the diseases selected for consideration in Dr. Tatham's reports, and while agents other than decomposition products are also responsible, its incidence in the occupational groups dealt with in the earliest chapters will form a rough test of some of the above statements. The comparative mortality figures for these occupational groups are given at the end of this chapter.

Certain inorganic substances, capable of irritating the tissues—

and of destroying them, when the products will have an irritative effect of their own—have caused abnormal growth. Irritation of a simple ulcer of the tongue with caustic has resulted in cancer, and in the few cases related by Fauvel in which laryngeal papillomata become malignant after removal, there was long-continued cauterisation with caustic subsequent to the operation. After swallowing caustic potash, a boy suffered from cancer of the stomach, and cancer of the œsophagus has followed the ingestion of a strong acid. Keloid has appeared upon the face after injury with lime, and it may be produced by the irritation of blisters. These facts prepare us for the reception of the suggestion which has been made that mustard and highly-seasoned foods play a part in starting cancer of the anterior part of the alimentary tract. The Germans in Buffalo may suffer from the seasoning in sausages.

In some parts of India continuous chewing is practised by practically every native, and cancer of the cheek occurs frequently at the place where the plug is kept. Into the composition of the plug enter betel leaf, tobacco, slaked lime, and areca nut or other spices. Some have it that the frequency of cancer is increased in districts in which more lime is used in the plug. Fells, on the other hand, ascribes the greater frequency to the practice of submitting the tobacco to a preliminary soaking in a thick, black syrup prepared from a crude sugar, this being followed by drying at the roadside.

Comparative Mortality Figures for Bronchitis.

Occupational Group.	1890–2.	1900–2.
Chimney Sweep, Soot Merchant	194	92
Gasworks Service	163	67
Indiarubber, Guttapercha Worker, &c.	—	59
Tallow, Soap, Glue, Manure, &c., Worker	144	36
Coach and Cab Service, Groom, &c.	137	66
Carman, Carter, &c.	172	83
Butcher	92	54
Fishmonger, Poulterer	125	53
Innkeeper, Publican, &c.	96	55
Inn, Hotel Servant	136	78
Maltster	102	27
Brewer	132	95
Average	136	63·5
All Occupied Males	101	53

CHAPTER X.

MECHANICAL TRAUMATA AS CAUSES OF MALIGNANT AND INNOCENT GROWTHS.

AS I desire to make this work a fairly complete study of the etiology of cancer, I will leave the path which has so far been rigidly followed, and enter into the consideration of other causes than those with which I have already dealt. By doing so we gain a strong advantage, for it is from a study of one of these causes that we get the clue to the nature of that direct, non-inflammatory action in the causation of cancer and other neoplasms which has been hinted at in previous chapters. But for this we must wait.

More frequently in the causation of sarcoma than of cancer, and perhaps least of all, of innocent tumours, mechanical traumata play a part. As the result of a severe blow the tissue cells become crushed, and along with the extravasated blood will decompose. Slight and transient friction acting upon skin and mucous membrane causes transitory hyperæmia ; more severe and prolonged, it results in inflammation, and even ulceration ; most intense, in necrosis. This recital of the inflammatory effects of mechanical traumata must not be allowed to stand in the way of a realisation later of their direct effects.

An effect of friction is to aggravate an inflammatory lesion initiated by another form of agent, and to prevent the healing of an ulcer.

Malignant Growths.

Cancer may be the sequel of a blow, but one resulting in a contusion rather than a lacerated, incised, or punctured wound. Though much damage may be done to sub-dermal tissues by a contusion, so that inflammation runs a prolonged course, the tissue from which the cancerous growth arises, the epithelium, may remain intact. I have found a record of one case of melano-sarcoma due to a prick, and it is possible that the melano-sarcoma developing so frequently in the feet of African natives is caused by punctures. It has been pointed out that melano-sarcoma often develops in the fingers at the site of frequent puncturing by the sewing-needle. Sarcoma is a familiar sequel to fractures, and to injuries due to blows, wrenches, sprains, &c., especially, I should say after reading clinical records, injuries involving hæmorrhage.

There is a considerable amount of evidence implicating friction, pressure, or slight injuries often repeated, as causes of cancer.

The causative relationship between cancer of the lip and the short, unwaxed clay pipe is clear and unmistakable. It has been pointed out that the stem becomes hot and dries the epithelium of the lip sufficiently to make the pipe and epithelium stick together, the pressure of the lip upon the stem aiding. On separation, a portion of the epithelium may be pulled away, and this happening at the same place so frequently, a pipe-sore may develop. This account can be qualified: firstly, repeated traction upon the epithelium may be a sufficient cause of inflammation without the pulling away of tissue; secondly, the pressure of the pipe upon the lip may act directly.

The irritation of broken, decayed, irregularly-shaped, or tartar-covered teeth induces ulceration of the lip leading to cancer. Other causes of lip cancer which have been operative are the constant chewing of a toothpick, the playing of wind instruments, repeated shaving with a dull razor, and drawing the cord of a net through the mouth in the case of fishermen. Tillmann noted that carcinoma of the lip in horses generally occurs at the corners of the mouth, where pressure is exercised by the bit.

Abnormal teeth, such as cause ulceration and cancer of the lip, may also induce similar conditions of the tongue, and other causes are repeated biting of the tongue, and fretting by the jagged end of a clay pipe. In three lathers Dennis recorded cancer of the tip of the tongue, which was used to rapidly push out nails kept in the mouth. Da Costa records a similar case.

The irritation of a badly-fitting or broken tooth-plate, or a jagged, projecting tooth, brings on chronic stomatitis which may culminate in local ulceration and cancer.

Calculi in the gall-bladder and duct, in the pelvis of the kidney, in the urinary bladder, and in the pancreas—all causes of cancer—are provocative of inflammation, and where they are preceded by and are due to such a condition, they must aggravate it. Scybalæ may induce ulceration, and probably are concerned in increasing the frequency of cancer in the large intestine. They sometimes lie in the cæcum for months at a time, keeping up a persistent irritation.

Cancer at the place of impact may follow the habitual use of a catheter, and epithelioma of the rectum is reported in patients using an injection syringe so as daily to bruise or lacerate the mucous membrane.

Inflammation due to irritation is presumable in the following forms of trauma which have been identified as causes of cancer: perforation of the tongue by a fish-bone, extracted fifteen days later; continued presence in the throat of a fish-bone or awn of barley; harbouring of a piece of straw in the eye for a period; wearing of spectacles, and especially of pince-nez, acting upon the base of the nose; the unsuspected presence of needles in the breast; wearing of tight belts; regular impact of the body against a machine;

friction of the saddle upon the scrotum among Mexican muleteers, as reported by Schaffner ; irritation of warts and moles ; fretting of scars ; the presence of a callosity upon the hand, the effects of further irritation presumably being added ; and scratching of the anus in cases of pruritis.

Innocent Growths.

In some of the examples given below the traumata are powerful enough to produce well-defined inflammatory states, but in others, if inflammation results, it must be of an exceedingly mild form ; and, indeed, I am of the opinion that we must look in these cases rather to direct, non-inflammatory action alone. Callosities and corns appear to me to be examples of abnormal growth of some significance, for hypertrophy in the case of both is a direct result of friction and pressure.

Keloid—again using the term in a liberal sense—appears after injury, including wounds caused by flogging, by burns, by leech-bites, and by piercing the ears for the reception of earrings. It has manifested itself in the sternal region, where seborrhœic eczema has provoked scratching, though it may begin spontaneously in the lesions of eczema. The inception of keloid in non-traumatic inflammatory lesions, and the observation of Strachan upon the relative frequency in the West Indies with which surgical scars took on keloid action in the pre-antiseptic days, might be taken as proofs that the only action of the traumata is to lay open the tissues to the attack of bacteria, and certainly they are proofs that the latter is an important factor ; but reasons will transpire why we should suspect the direct potency of the traumata.

Polypi of the gum have originated from irritation by the ragged edges of teeth and by artificial tooth-plates, and injury to the alveoli by the extraction of teeth has resulted in the development of epulis (an elastic term), while polypi may spring from the tooth pulp after fracture of healthy teeth. To the presence of ground glass in snuff have been ascribed nasal polypi, and they have also been attributed to blows. A patch of villous polypi has been found in the bladder at a spot impinged upon by a piece of straw four and a half inches long, and papillomata have appeared where the apex of the bladder was in contact with a large oval calculus. Simple adenomata of the rectum appear in children in cases of prolapse. On the noses, gums, palates, and feet of sheep pasturing on clover in stubble are recorded warts due to the irritation of the latter.

Lipomata are traceable in some cases to local irritation, as by the suspenders, and Park has it that they are usually traumatic, the injury being slight and long forgotten. He also asserts that fibromata are usually traumatic, and that the majority will be found to contain minute foreign bodies (slivers, splinters, &c.). In horses, subcutaneous fibromata are said to appear where pressure is exercised by the harness. Molluscum fibrosum is said to appear most frequently at places exposed to irritation, and other neurofibromata are determined by injury or pressure. Intermittent pressure or friction over a bone may produce exostoses, and of course drill-bones must not be forgotten. Angiomata sometimes follow injuries and other traumata, especially in the form of a pinch, and telangiectases occasionally follow slight injuries.

In many of the occupations in the table the workers will be exposed to special forms of mechanical irritation, but to determine the incidence of cancer with respect to these will prove a most difficult task.

CHAPTER XI.

SUNLIGHT, RONTGEN RAYS, AND EXTREMES OF TEMPERATURE AS CAUSES OF CANCER.

TO the action of these physical agents inflammation may be a sequel, and of their potency in causing cancer there is a little evidence. Sunlight and extremes of temperature can reasonably be suspected of adding their effects to those of other agents in causing cancer of exposed parts and even warts in these situations.

Not all the evidence is given in this chapter ; some will also be found in Chapter XVI.

Sunlight.

Sunlight, or rather the actinic rays of sunlight, acting upon the skins of predisposed persons, can produce even the most severe forms of inflammation. It also encourages the development of eczema. Yet I do not lay stress upon an antecedent inflammation in cases of cancer due to the actinic rays. Where it occurs, it must be very slight in its effects.

Shield recorded the case of a man who, as a boy, had a fair complexion. The sun used to scorch and hurt his skin, so that his hands, face, and neck would turn red all over, and would burn and " swell." In the course of time numerous dark patches appeared upon the skin, especially of the face, and later a number of carcinomatous growths developed in the sweat glands of the face and neck. This may have been xeroderma pigmentosum.

Xeroderma pigmentosum, which invariably has cancer for a sequel, begins sometimes as a chronic erythema of the skin in exposed parts of the body. The inflammation is more intense in the summer, and is undoubtedly due to the action of sunlight.

Unna's " sailor's skin," which some call the xeroderma pigmentosum of adults, is also found upon exposed parts of the body. It culminates in cancer, and there is an antecedent erythema. It is ascribed by Unna to vicissitudes of the weather, but it may be due in part to the action of sunlight, a belief which is encouraged by the existence in it of abnormal conditions of pigmentation. However, I am unable to exclude the action of wood-tar also, with which the sailor comes frequently into contact. That the disease appears upon the face and ears as well as the hands is no difficulty, for the hands are frequently applied to these parts, and as regards the pigmentation, it must be remembered that melanoderma occurs among workers in pitch and tar and among gasworkers. I do not press this point, for the reason that the disease so strongly resembles xeroderma pigmentosum, where this cause is excluded, that the action of the tar can only be an accessory one.

Rontgen Rays.

These rays can induce a chronic dermatitis which may proceed to ulceration. Chronic X-ray dermatitis is in some respects similar to xeroderma pigmentosum.

Now familiar is the supervention of malignancy upon X-ray dermatitis and in the lesions of lupus vulgaris treated by the rays. Lardennois asserted that certain epitheliomata were aggravated by them.

Extremes of Temperature.

The prolonged action of heat upon the skin, according to its intensity, results in inflammation, leading even to ulceration, and, of course, severe transient heat has pronounced effects. Extreme cold manifests its results in chilblains and frostbites. The thermal rays of sunlight, as well as the actinic, and cold, especially combined with wet, are said to predispose to eczema.

Cancer of the œsophagus and stomach have followed upon the swallowing of scalding hot water. Hot food and hot tobacco smoke are credited with being agents in the causation of cancer of the tongue, but I would like to know what is the proof of this. The suggestion has been made that the heated end of a pipe induces cancer of the tongue. The short-stemmed clay pipe may be potent in cancer of the lip in some cases partly because of the inflammatory effects of heat, though in others its effects must be exercised directly. In those cases of cancer of the face already mentioned where blame has been given to sunlight, the thermal rays may also have been operative.

Wyeth asserted that cancer of the external ear most commonly results from frostbite, and is comparatively rare in women, and, according to Butlin, it is more frequent in men who follow occupations which expose them to the weather. Cancer of the lip occurs frequently in outdoor workers; but in both cases how far is the weather responsible, and how far the sunlight? Further, the free use by outdoor workers of the short clay pipe must increase the incidence among them of cancer of the lip.

We must not forget here the doubtful example of Unna's "sailor's skin" as an effect of extremes of temperature.

The frequency of cancer upon the Mexican tableland may be due, as has been suggested, to the very changeable temperatures characteristic of that region. Wolff suggested that the very low incidence along the Mediterranean shores of France is explicable as a result of equable temperature.

The workers in some of the occupational groups considered in the earlier chapters, gasworkers and drivers of vehicles in particular, will suffer from extremes of temperature. The "lipoma nasi" of cabmen owes its development in some cases partly to the weather, and in other cases this may possibly be the only agent.

A very curious example of epithelioma occurring in Kashmir may be considered here. It develops on the abdominal wall or the inner surfaces of the thighs, and is ascribed to irritation by the kangri, or fire basket. For heating purposes an earthenware bowl is suspended in basket-work below the clothes and next to the skin. Drift-wood is preferred as fuel, but charcoal and cow-dung are commonly used. When the native is in a standing position the kangri hangs against the abdomen; in a sitting position it is placed between the thighs. He does not keep his skin very clean. Here are a number of possible agents: heat, friction and pressure, heat decomposition products and dung. Of course, it is only those upon the spot who can decide which are potent. The ulcer which develops owing to the use of the kangri is credited to repeated burns and chronic irritation.

CHAPTER XII.

Neoplasms due to the Attentions of Animals.

INFLAMMATORY conditions—temporary, yet sometimes lasting—are induced by the bites or stings of insects, and they result from the presence of worm parasites in the body. Many cases are on record where most severe and prolonged local effects have been caused, even by the former. It is therefore not surprising that references are to be found to cases of abnormal growth due to their action, though these are not numerous.

Woolley recorded a case of a labourer who was stung, or bitten, on the forearm by a "green fly" six months previously to his seeking advice. A tumour had developed, which was not adherent to the tissues below. When excised and examined, it was found to be a squamous-celled epithelioma with well-developed cell-nests. The occurrence of calcified epithelioma, due to the sting of a wasp, is mentioned by Unna. Tillmann asserts that in cats the upper lip is more usually carcinomatous because of repeated bites by small animals. The most serious of the local effects in cases of bites or stings are of course due to irritating fluids expelled by the animals, but the puncture may have its potency, for malignant growth can follow upon a prick.

Certain cases of cancer and sarcoma in mice were ascribed by Borrel to irritation by cysticerci and to the presence of nematode worms in the neighbourhood. Pepper asserted that echinococci and cysticerci present in the cranium sometimes give origin to tumours. The ova of Bilharzia, becoming lodged in the finer blood-vessels, may produce polypoid fibro-adenomata of the bladder and polypi in the rectum. They have also received the blame in epithelioma of the bladder.

Loeb mentioned the endemic occurrence among the cattle in the Chicago stockyards of epithelioma in the inner angle of the eye. This is very suggestive of the attentions of an insect.

Elsewhere are mentioned cases where keloid developed after leech-bites and the bite of a centipede.

CHAPTER XIII.

CANCER OF THE UTERUS AND MAMMÆ.

A STUDY of the incidence of cancer in women affords strong confirmation of the hypothesis which seeks to identify irritative conditions as the antecedents of cancer, and there is no stronger fact before us than that the uterus and mammæ, which stand out prominently from other parts of the female body with regard to their proneness to become cancerous, are the most liable to irritation.

Take first the case of the uterus. The direct evidence of a causative relationship between cancer and non-traumatic inflammatory conditions or traumata is not very strong. In some cases chronic uterine catarrh has preceded ; lacerations of the cervix have been provocative in others, and some recent American workers leave us to suppose that there is no other cause. Tissue changes from flexions and irritation by the remnants of puerperal sepsis have been blamed. Cancer is said to develop in " uteri long or often ulcerated," the causes of the ulceration not being mentioned, while it has appeared in the seat of a syphilitic ulcer in the cervix. Cervical cancer may follow the use of a pessary. In some cases of uterine cancer there has been a history of miscarriages, upon which inflammation frequently follows.

It is only in a minority of cases that the finger can be placed upon a precancerous condition or definite source of irritation, but the indirect evidence is very strong. The incidence is high among multiparæ, and among the cancerous multiparæ is frequently to be found a history of protracted and instrumental deliveries. In all women, and especially in multiparæ, cancer develops more frequently in the cervix than in the body of the uterus, and it is the cervix, of course, which receives injury during delivery. The claim has been made that cervical cancer is almost exclusively confined to women who have been pregnant, and also that ulceration and cancer of the uterus are both less frequent among coloured women in the United States than among the white women.

We may recall how frequently uterine inflammation appears after confinements, sometimes as a result of exploratory and other instrumental erosions and injuries, and how persistent are lacerations of the cervix, which sometimes last a whole lifetime unless operated upon. Blood, debris, &c., remaining in the uterus after delivery will decompose and render inflammation more possible ;

and after delivery the uterine tissues shrink, when autolysis must ensue, if not some degree of bacterial decomposition.

Increasing the special liability of the cervix is the use of caustics, and, maybe, the injection of irritating fluids. The cervix is the favourite seat of gonorrhœal inflammation, there being a history of gonorrhœa in some cases. In the case of carcinoma of the fundus it has been remarked that there is " good ground for believing that the metritis of gonorrhœal infection is a predisposing factor." The objection may here again be raised that cancer is relatively rare among prostitutes. I have already drawn attention to the shortness of their lives, and to the effect of marriage in reducing the proportion of older women following this life, and I now can point out that they are generally sterile or relatively infertile, so that they must be less subject to the irritative influences mentioned above.

Turning to the nulliparæ, we find that cancer, relatively rare amongst them, attacks the body of the uterus more frequently than the cervix. Directly after the close of the menstrual period, owing to its shape the uterus may retain much blood and exfoliated mucous membrane, which will decompose and provoke inflammation, and periodical breaking-down of the membrane in the areas thus weakened will make matters worse. This factor, of course, holds also in the case of multiparæ, but in them the frequency of cancer of the body of the uterus is overshadowed by the frequency of cervical cancer.

As in the case of the uterus, the direct evidence connecting mammary cancer with inflammation and irritation is not very strong. In some cases chronic interstitial mastitis is reported, without the causes of the inflammation being specified (they are sometimes traumatic), but in a few only of these cases has it been proved that the cancerous growth began within the seat of the lesion. Old abscesses have become cancerous. Paget's disease of the nipple, and fissured and ulcerated nipples, are familiar precancerous conditions. Antecedent blows are mentioned, in some cases followed by extravasation of blood ; squeezes and friction of the corset or its strings have been operative in others. Paget's disease, friction, and blows are given the credit in some cases of cancer of the male breast. The above causes are implicated in a minority of cases only. When we turn to the indirect evidence it will not prove to be very strong.

The incidence of cancer of the breast is very little higher among married than among unmarried women, though I would like to be assured that there have not been included among the latter women who ought to have been married. Owing to very early weaning of their children this class must suffer profoundly from the effects of retention of the milk. This small difference between married and unmarried women is partly to be expected, for the breasts are subject to irritation other than that incidental to child-rearing. The most frequent site of malignancy is the upper, outer part of the breast, where it is most exposed to traumata. Several authors have noticed the more frequent occurrence of mammary cancer on the right side, and this is true also of diseases predisposing to cancer, such as puerperal mastitis. Cancer of the breast and chronic mastitis both begin to increase in frequency after the menopause. During that period and after each period of lactation there is autolysis of part of the glandular elements.

CHAPTER XIV.

ARSENICAL CANCER. THE NEUROTIC HYPOTHESIS.

UP to this point organic compounds only among the chemical agents have received notice, but there is at least one inorganic compound—arsenic—which is an agent.

According to Paris, cancer of the scrotum, due to the action of arsenious acid, occurred in copper and tin smelters. Yet Butlin, inquiring in Cornwall, could not find record of a single case.

Rayer reported cancer, preceded by dermatitis, among the smelters of arsenical ores.

Hesse reported that cancer of the lungs—described also as lymphosarcoma—was not uncommon among the cobalt miners of Schneeberg, in Saxony. The dust of smaltite (cobalt arsenide) received the blame, and the air of the mines was laden with it. Ores containing sulphur were less potent. Among the 600–700 men employed, the deaths annually were 28–32, of which 21–24 were from cancer.

The Cornish copper and tin ores contain arsenic in sufficient quantity to be worth extraction for its own sake. Unfortunately, the number engaged in mining these ores is not sufficient to render the statistics of any value. These statistics are : copper miner [cancer—99 (51), 39 (63)] and tin miner [cancer—58 (51), 68 (63)], but in the case of the former there were three deaths only from cancer during the first period and one during the second, in the latter twelve during the first and ten during the second. These miners suffer from lung affections of a doubtful nature, which cannot be determined owing to a difficulty in obtaining post-mortems. I am in doubt whether or not the smelters are included, and they seem to suffer more severely from the effects of arsenic than the miners. Ventilation in the mines is not too perfect, and the respired air and decomposition products from the lamps may be potent.

In the Prussian town of Reichenstein, where arsenical mining is an important industry—and, I expect, smelting also of the ores—Geyer found some cases of carcinoma of the fingers, supervening upon arsenical "warts." Many of the inhabitants suffered from arsenical poisoning due to arsenic-containing water.

A number of observers—led by Hutchinson—have reported the onset of epithelioma in psoriatic patients who have gone through a long course of arsenic. In some cases the epithelioma began in the psoriatic lesions, but in others it was preceded by growths, situated on the palmar and plantar surfaces usually, but also elsewhere, which have been called warts or corns apparently according to their prominence ; some were horn-like. These growths sometimes appeared in the psoriatic lesions. I am not aware of any histological work which proves that hypertrophied papillæ enter into their composition, or that they are more than epidermal growths, each set around the opening of a sudoriferous gland, so that an attempt to place them on equal terms with warts is futile. From our point of view it is enough that they are abnormal growths. An earlier statement that cancer develops in psoriatic lesions requires some degree of qualification in view of the above facts.

By impinging directly upon the skin and mucous membranes, or by first becoming absorbed into the blood, arsenic has decided irritative effects. Among the miners the arsenical dust induces inflammatory conditions of the gastro-intestinal tract. Owing to the action both of fumes and dust, the smelters and calciners of arsenical ores suffer in the same way, and from irritative conditions of the respiratory passages, as well as from eczematous eruptions, which may result in nasty sores, about the genitals and exposed parts of the body.

In the cases mentioned by Rayer, a preceding inflammation was noted, and where epithelioma begins in a psoriatic lesion, the inflammation will be aggravated by the arsenic, which is known to happen.

Thus arsenic may be ranged alongside the decomposition products as a potent agent. It is active when circulating in the blood, so that we can more readily believe the volatile decomposition products to be active when inhaled.

So far I have omitted to mention how the direct effect in impairing the control of growth is exercised by the various forms of trauma—chemical, mechanical, and physical—and by the inflammatory products. My suggestion is that this effect is the impairment of the control of the nervous system upon tissue growth. This is not a new hypothesis, but it has received the scantest notice. Maybe the reason has been that we are without proof of a trophic function, pure and simple, of the nervous system, and certainly it is generally agreed that special trophic nerves do not exist. To this long-debated question of a direct trophic function, a control over tissue growth, I may add the evidence contained in the following pages. Taken as a whole, it is nearly as good a proof that nerves exercise a direct trophic function as it is of the neurotic basis of cancer. As I include connective-tissue tumours in the survey, objection will be made that a nerve-supply to connective tissue is absent, but the consensus of evidence in favour of the neurotic hypothesis of the origin of all kinds of neoplasm is so strong that I believe this difficulty will some time be explained away.

It was on finding that arsenic was concerned in the causation of cancer that my attention was turned in this direction. Learning its therapeutical uses, I could only form the conclusion that its potency as a cancer agent depended upon its neurotic effects. In certain quantities it is a tonic, but, like all other nerve stimulants, the action is depressant after too prolonged a use or in excessive doses. Workers in occupations in which arsenic is mined, extracted, or used in manufacturing processes, or persons ingesting excessive doses of it, all suffer from nervous derangements : headache, nausea, anorexia, diarrhœa, drowsiness, debility, depression. Paralysis may also result. The internal administration of arsenic may induce a state of abnormal pigmentation of the skin and hyperkeratosis (the nervous basis of which will be considered later) and herpes may also develop. Small doses may keep the peripheral nerves in a state of excitement, but a more severe course causes peripheral neuritis, and sometimes a pearled state of the dendrites in the cortex. Arsenious acid is used as a gastric sedative.

CHAPTER XV.

THE NEUROTIC BASIS OF CERTAIN ABNORMAL CONDITIONS.

TO look into the effects upon the nervous system of the other agents concerned in the causation of cancer would appear to be the next step; but there are certain subsidiary phenomena—manifested in some neoplasms and in certain precancerous conditions, or otherwise accompanying the neoplasms—some of which can be evoked by the action of certain of these agents, and it will simplify matters if first these phenomena are proved to have a neurotic basis. The phenomena in question are abnormal pigmentation of the skin, hyperkeratosis, abnormal conditions of the hair, telangiectases (themselves neoplasms), and hypertrophy of parts of the body, especially hemihypertrophy.

There are a number of reasons why attention should be paid to the cause of abnormal pigmentation of the skin other than that which is due to deposits of altered hæmoglobin. The inception of a melanotic tumour of the skin may be as a thin layer of pigment without the appearance at first of tumour formation. Hutchinson noted that in cases of epithelioma of the eyelids the patients are usually elderly women who have long suffered from crops of freckles in the neighbourhood; one of the freckles becomes first warty and then epitheliomatous. Little had a case where juvenile flat warts seemed to have developed in the sites of freckles. Abnormal pigmentation is one of the earliest appearing features of certain cancerous conditions: xeroderma pigmentosum and Unna's "sailor's skin." The abnormal pigmentation in naevi must not be forgotten, nor that present in von Recklinghausen's disease (neurofibromatosis) and senile keratosis.

That disturbed innervation doubtless plays the chief part in abnormal pigmentation of the skin has long been recognised. Abnormal pigmentation may appear as the result of peripheral neuritis or of degenerative changes in the spinal chord. In some cases of leucoderma changes have been found in the nerves supplying the pale patches of skin. Abnormal pigmentation may be unilateral and have middle line limitations, and it may be distributed in nerve territories. It is one of the stigmata of degeneracy. It may be due to reflex action; for example, chloasma resulting from chronic uterine irritation and appearing also during pregnancy, and increase of pigment in the areola during the latter condition. The bronzing of the skin in Addison's disease is said by some to be due to irritation of the abdominal sympathetic, though others assign different causes. Alexander had a case of symmetrical pigmentation of the skin accompanied by anæsthesia of the pigmented patches.

Attention may be drawn to the rare disease acanthosis nigricans, where warty growths appear within pigmented areas which are usually symmetrical. It is thought that the lesions are of reflex origin.

Pigmentary changes in the hair have a neurotic basis. Changes in colour are familiar as a result of cerebral disease, injuries to nerves, neuralgia, neuritis, and pronounced emotion ; and in some cases of traumatic neurosis the hair very quickly turns grey. Cheatle found that when colour-changes occur in the hair of the face in males, they may stop short at the boundary of the area of distribution of a cutaneous nerve. In one case the hair of the beard had become white within the area supplied by the mental nerve, and in another the hair in this area had remained normal, while the whiskers were white. In yet another case whiteness began in the mental area on both sides over points where cutaneous nerves came to the surface, an observation which will be better appreciated later. Cheatle has noticed a similar feature in other cases, and he has also pointed out that in infantile or congenital greyness of the hair, the abnormal patches appear over such points.

The condition of hyperkeratosis is characteristic of some forms of precancerous lesion and of certain innocent growths. Of the former keratosis linguæ and senile keratosis are familiar examples ; and hypertrophy of the horny layer occurs also in xeroderma pigmentosum and Unna's "sailor's skin." Abnormal proliferation of the horny layer is found in warts, angiokeratomata, and some forms of pigmented naevus; and Unna noted that symmetrical palmar and plantar keratosis may coexist with more or less numerous naevi. Hyperkeratinisation is the characteristic feature of corns and callosities, and it is manifested in acanthosis nigricans.

There are some grounds for believing that hyperkeratinisation depends upon nerve derangement. It is found in ichthyosis and other potentially symmetrical skin diseases with a neurotic facies. Local horny thickenings have been observed as sequels to nerve injuries and during the course of tabes dorsalis, and though the intermediate cause suggested is venous stasis, this is incredible. The prolonged hyperidrosis of the palms and soles common in neurotics, excessive drinkers of tea, and alcoholics may be followed by a considerable degree of hyperkeratosis ; and in the case of hyperkeratosis of the same region due to the excretion of arsenic by the skin, chronic local hyperidrosis is a frequent concomitant and may precede it. The symmetry is significant.

For the reason that the skin above pigmented and vascular naevi generally presents abnormal conditions of the hair, it may fairly be urged that the cause of the development of the naevi will be of the same nature as that underlying the development of these conditions. Abnormal states of the hair may take different forms—increase or decrease in the number of hair follicles, increased growth in length or thickness, persistence of lanugo hairs as the hairy coat, excessive falling out or retention of hair which would otherwise fall out—but the evidence obtainable does not always particularise, and general terms are often used. It is true that some only of the above conditions are characteristic of naevi, but most, if not all, depend upon the same cause—here again a neurotic one.

There may be abnormal growth of the hair after injuries to nerves or following upon central lesions. In spina bifida occulta, a spinal nerve may be involved in fibrous tissue, or compressed by an accumulation of fat, when a mass of long hair may appear over the lower limbs and back. The hair of a part the seat of neuralgia may overgrow. Women have become hairy during each pregnancy, and have lost the hair between whiles, a phenomenon which may be placed alongside chloasma on the ground that it is due probably to the same interposing cause. In cases of nervous debility the hair falls away, and it may be lost suddenly as a result of a mental shock. Abnormal hair conditions are among the stigmata of degeneracy, and they are hereditary. Changes of season, acting through the nerve-centres, induce in animals changes in their coats and plumage. Virchow noted that in " wild men of the woods " the most essential changes lie in the region of the trigeminal.

While vascular naevi are usually congenital, telangiectases are acquired. The latter have been called capillary naevi, and their anatomy is sometimes very similar to that of the simpler forms of vascular naevi. The most marked feature in which the two forms of new growth differ is that in the telangiectasis proliferation of the blood-vessels is not so prominent. Telangiectases appear in the lesions of xeroderma pigmentosum and Unna's "sailor's skin," and accompany certain other forms of multiple neoplasm.

Vidal has it that generalised telangiectases are of neuropathic origin. They are sometimes symmetrical, and they are among the stigmata of degeneracy. As their appearance is sometimes heralded by local hyperæmia, suspicion may therefore be directed towards the nervous system. Among the stigmata of exophthalmic goitre are erythematous flushing and telangiectases.

On page 74 will be found additional evidence.

Hypertrophy of parts of the body, especially when it is unilateral, has an interest for us. Innocent neoplasms seem frequently to be associated with hemihypertrophy. And what are neoplasms but examples of circumscribed hypertrophy?

Here, again, there is proof of a neurotic basis. It is established that irritation of the trigeminal, either at its origin or in its course, plays a part in the development of acquired facial hemihypertrophy. In several instances it has begun during or after the course of inveterate trigeminal neuralgia, and in some cases it corresponded with the distribution of that nerve. With congenital cases mental defects are associated with comparative frequency. Increased flow of saliva and increase of perspiration have been noted upon the affected side, especially in congenital cases, and in one there was increased growth of the hair upon that side. Upon the affected side have also been observed sensory abnormalities. Hypertrophy of the jaw of one side was noted by Schiff after section of the inferior maxillary nerve. With this may be compared the hypertrophy of the ear in rabbits which sometimes ensues after section of the cervical sympathetic or of both sympathetic and spinal nerves. Fœtal meningitis has been suggested as the cause of congenital facial hemihypertrophy. Barwell has ascribed facial hemihypertrophy to perverted or imperfect action of the sympathetic of the neck.

A deformity of the lower limbs resembling elephantiasis occurs in tabes, and an hypertrophied condition is also seen in syringomelia.

Acromegaly will repay study. This disease is generally symmetrical, or nearly so, but it may be definitely unilateral. The skin is usually thickened, its pigmentation may be increased, and the hair is sometimes abnormal. In most cases there is increased perspiration, and in some increase of the sebaceous and lachrymal secretions. There are other neurotic symptoms, and the symptoms appearing before the signs of increased growth are also neurotic. The putative causes are all of them such as act upon the nervous system: severe fright, impressive events, mechanical trauma, poisoning with coal gas, chronic poisoning by alcohol and lead, syphilis, and typhus and other infectious diseases. In some cases there was acceleration in the progress of the disease after fright or mechanical trauma. That the hypophysis is diseased is an important point, for it is concerned in the welfare of the nervous system, and is diseased in many cretins. The consensus of evidence here repeated affords strong proof of the neurotic basis of acromegaly.

Acromegaly and gigantism—a phenomenon of degeneracy—have affinities, and a large proportion of giants are acromegalians, though a less proportion of acromegalians are giants. Some giants suffer from facial hemihypertrophy.

I cannot leave this part of the subject without drawing attention to the fact that upon lesions of the sympathetic nerves may follow abnormal pigmentation of the skin, increased growth of the hair, and hyperæmia, while the experiments may be again recalled in which hypertrophy of the ear followed in some cases upon section of the cervical sympathetic. We will find that the agents inducing cancer may affect the sympathetic system as well as the spinal. This is the case with arsenic.

CHAPTER XVI.

THE EFFECTS OF CANCER AGENTS UPON THE NERVES.

THE clue gained by a study of arsenical cancer and of the physiological behaviour of arsenic can be followed among the other forms of agent acting as causes of cancer and other neoplasms. For each form of agent decided effects upon the nervous system can be proved. Additional evidence of the causation of cancer, also of innocent growths, is here included.

Mechanical Traumata.

A blow, especially one leading to a contusion, may crush the peripheral nerves, and a state of chronic neuritis may follow, manifesting itself in neuralgic pains. Temporary local paralysis may result. The pain experienced is some indication of the effects produced by a blow, as also is the fact that reflex inflammation is sometimes caused. What is true of blows must also be true in a degree of friction or fretting. Acting over a long period, marked intracellular changes are produced in the ganglia of the posterior sensory roots, and Cheatle has suggested that it may induce profound physiological changes in the areas of their distribution as well as at the actual site of the irritation. Gall-stones, among other calculi, have decided effects upon the nerves. In addition to direct impairment of the nervous system, an indirect effect is produced by mechanical trauma, especially by constant irritation, for the disorganisation of the tissues or the impairment of their function, and the paralysing effect of the trauma upon the nerve-endings, will lead to an interruption, partial or complete, of the functional relationship between the tissues and the nerves, and the result of loss of function on the part of the nerves will be a tendency towards disorganisation. This indirect effect will also follow the action of other forms of trauma, and the suspension of the normal function of nerves supplying areas which are the seats of chronic inflammation, whatever be the cause of the inflammation, must be decided in degree.

When primary growths develop within the thorax as the result of a blow, an explanation feasible in a limited number of cases is that of reflex action. Perhaps a precancerous inflammatory condition is first induced, but in some cases of sarcoma the onset is so rapid that it must be due to direct action. Sarcoma so frequently develops almost immediately after a mechanical trauma, and a chronic inflammatory condition is so seldom associated with it, that direct action only on the part of the trauma can be possible.

It is remarked by Strümpell that "general traumatic neurosis seems sometimes to prepare the ground for the development of organic lesions, such as paralysis or tumours."

Sunlight. The Actinic Rays.

In moderation the actinic rays in sunlight have a tonic and stimulative action, but acting in excess upon individuals with an irritable nervous system, there ensue headache, sleeplessness, exhaustion, loss of appetite, &c. The actinic rays can induce local anæsthesia, and sunlight relieves nerve affections, scrofula, rickets, diabetes, and gout. Absence of sunlight in valleys has been suggested as a cause of cretinism. Sunstroke is a striking example of the neurotic effects of these rays, and red or orange screens are protective. The skin tans in sunlight, and in some individuals it becomes freckled. A notably symmetrical skin trouble, leucoderma, of which the first stage is an increase of pigment in certain regions, followed by the development of a white spot which appears to drive the pigment before it, occurs mostly in the tropics. In many cases it follows sunstroke, and the neurotic temperament and nerve-depressing influences favour its development. Hyperkeratinisation is another effect upon the skin, but hyperæmia is more familiar. It is extremely probable that the heat-rays in sunlight accentuate the neurotic action of the actinic rays, and that the luminous rays also are operative with them.

Dubreuilh studied the relationship between epithelioma and sunlight with the following results: senile keratosis—showing itself at first as blotchy, circumscribed pigmentation accompanying achromic atrophied patches, among which are often found fine dilated veins—occurs with the greatest frequency among those who live in the open air. It is found only on uncovered parts of the skin, and is probably due to sunburn. The ears, frequently attacked in men, are entirely free in women, who wear handkerchiefs over the head, and are affected only in those parts uncovered by the handkerchief. Upon the keratosis may develop epithelioma. Senile epitheliomatosis of the face affects farmers particularly, and all those who work in full sunlight. Blondes are much more frequently attacked than brunettes, coloured people least of all. The disease is essentially rural. Alongside these statements must be placed the assertion of Butlin that cancer of the external ear is more frequent in men who follow occupations which expose them to the weather; but, of course, they are also exposed to sunlight, and both agents may be responsible.

Hyde has cited evidence of a varied nature to show that the actinic rays are factors in the production of cancer in exposed parts of the body, and that the pigmented skin of negroes has a protective action.

In a case under the care of Colcott Fox, of a sugar planter who was much exposed to the sun for 30 years, the skin of the back of the hands was atrophied and rather livid, and it was pigmented and dotted with peculiar warts which, as Morris noted, were like those appearing after irritation by the X-rays. On one of the hands was growing what appeared to be a rodent ulcer. This case resembles xeroderma pigmentosum.

Some of the conditions holding during the course of xeroderma pigmentosum are worth recalling. There may first appear in successive summers erythematous patches, the effect partly of vaso-motor paralysis. After the beginning of the erythematous stage, which is not always present, and in that case as the commencement of the disease, there appear freckle-like pigmented patches, which become larger and darker. Then telangiectases develop, and hyperkeratosis also shows itself. Later appear flat warts, and these enlarge and fungate, becoming cancerous. If the erythema, telangiectases, abnormal pigmentation, and hyperkeratinisation are neurotic phenomena, why not the later stages ? In the early stages of Unna's "sailor's skin" appear erythema, telangiectases, abnormal pigmentation, and hyperkeratinisation. These conditions are suggestive of a neurotic basis. Is it not, then, a strong presumption that the later stages—large, warty outgrowths, hypertrophied sebaceous glands, and carcinoma—are also neurotic phenomena ?

Rontgen Rays.

The X-rays have an anodyne and analgesic action, and relieve pain in tabes, neuralgia, and rheumatism. Paraplegia, insomnia, epilepsy, and depression are ameliorated. They cure hyperidrosis or cause profuse sweating, and encourage the growth of hair or act as depilatories. Pigmentation of the skin may follow their use ; they also depigment. Vascular disturbances appear under X-ray treatment, and telangiectases are most characteristic of X-ray burns. Hyperkeratosis of the hands develops in X-ray workers, and the rays cure keratosis senilis. Sensation may be disturbed in the skin. Symptoms resembling those of sunstroke may develop after exposure to the rays.

Warts appear upon the hands of operators in X-ray departments, and are removable by the rays in more moderate doses.

Extremes of Temperature.

In a mild form heat is a nerve stimulant ; stronger in degree it causes depression. After prolonged and repeated exposure to severe heat, permanent damage to the nervous system, and even insanity, may result. Histological changes take place in nerve-cells on exposure of an animal to severe heat. Play of heat upon the skin is one of the causes of neuralgia. Heatstroke is induced by the direct action of heat upon the nerve-centres, and the predisposing agents are of the nature of nerve-depressants: fatigue, dissipation, illness, alcoholism, and overcrowding, and otherwise living in an impure atmosphere. After examination of the pertaining evidence, I have failed to see why the separate entity of heatstroke and sunstroke should not be admitted, though in the case of sunstroke it is exceedingly probable that the rays of heat sometimes act along with the actinic rays.

A moderate degree of cold is stimulative; an excessive degree is depressant, and, according to its intensity, there may appear symptoms like those of alcoholic intoxication and drowsiness or torpor. Cold is a tonic to the nerves of the skin; in excess, as when ice is used, it is sedative and anæsthetic. The shock of cold air upon the lungs enfeebles or paralyses the vagus, and by reflex action induces nausea, vomiting, or disturbances of digestion. Peripheral neuritis, especially of the facial, is one of the effects of exposure to cold winds. I have found a reference to "cold freckles," without as yet obtaining details.

It would be interesting to know whether or not it is really the case that scars left by severe burns and scalds are more liable to become cancerous than other scars, for the shock to the nervous system is profound, and these scars are usually quite insensitive.

It is said that telangiectases tend to appear upon the faces of those much exposed to the inclemencies of the weather. We have already seen that they occur in xeroderma pigmentosum, which is due to the action of sunlight, and therefore the same cause may operate alone when they appear by themselves. Yet extremes of temperature, acting upon the skin, have neurotic effects as well as sunlight, and telangiectases apparently have a neurotic basis; thus, extremes of weather may play a part as well as sunlight, acting along with it, in causing the formation of telangiectases. Keratosis of the lips is said to appear also in those exposed to the inclemencies of the weather, but Dubreuilh's work indicates sunlight as the agent in senile keratosis. Yet it may be that the inclemencies of the weather act along with sunlight in inducing keratosis of the lips, for heat undoubtedly causes the hyperkeratinised condition of the lips, leading, maybe, to cancer, which sometimes follows upon the use of a short clay pipe.

Some extreme examples of callosity have been ascribed to the action of heat. The neurotic action of cold encourages the development of "lipoma nasi" (rhinophyma), though it is certainly due also to reflex action from the stomach.

Decomposition and Inflammatory Products, &c.

Of the depressant and other action of heat decomposition products I have before me a very considerable mass of evidence. Drowsiness, lassitude, debility, headache, nausea, anorexia, vomiting, vertigo, &c., are induced by prolonged and repeated inhalation of purified coal-gas and the emanations from gasworks, hydrogen bisulphide, carbon monoxide and dioxide, the vapours of mineral oils, benzene, nitrobenzene, aniline and carbon bisulphide, and the fumes evolved during the distillation of tar.

Continued inhalation of ammonia causes debility. Cyanogen compounds are depressants, and hydrocyanic acid is a local sedative. Acute narcotic symptoms follow the inhalation of carbon monoxide and the vapours of the fatty hydrocarbons, benzene, nitrobenzene, aniline and members of the pyridine and quinoline series, as well as upon the swallowing of these liquids. Many, if not all, of the volatile fatty hydrocarbons, and benzene and carbon bisulphide, when inhaled, produce general anæsthesia; and carbolic acid, wood-tar creosote, and carbon dioxide induce local anæsthesia in mucous membranes. As carbolic acid can be absorbed through the skin, it can therefore lead to the formation of warts, through the medium of a local paralysis of nerve-endings, though it is possible that inhalation of the vapour is also responsible, for it is then depressant and induces debility. Carbolic acid also paralyses nerve-centres. Neuralgia occurs not seldom in gasworkers, and the continued inhalation of purified coal-gas leaves behind permanent effects upon the nervous system, while the continued inhalation of benzol or carbon bisulphide causes peripheral neuritis, which appears among rubber workers. Chimney sweeps are liable to have hyperkeratinised skins; gas, tar, and pitch workers suffer from melanoderma; and aniline workers from hyperidrosis. Gas-workers are said to be prone to chronic rheumatism owing to their exposure to high temperatures, but can we be sure that the decomposition products are not also responsible by their action upon the nerves? Unless I am mistaken in reading the signs of the times, the state of the nerves predisposing to rheumatism is beginning to receive more attention.

The depressant conditions due to smoking are familiar enough. In tobacco smoke there is much carbon monoxide, which is a powerful narcotic; and, of course, nicotine, pyridine, and most of the other constituents are also narcotics. The smoke affects the nerve-endings in the mucous membranes of the mouth and throat. Its effects upon the nerve-endings in the tongue can be immediately appreciated upon drawing at a cigar or pipe.

The emanations from soap, tallow, glue, and manure works, and from sewers and damp cellars, the air of stables (especially when entered at the beginning of the day), and "impure air," all have some depressant and other nerve effects: headache, nausea, anorexia, vomiting, malaise, lassitude and debility. Bad ventilation and lassitude are as cause and effect, and impure water induces debility. "The peculiar sickening odour from decomposing matter is specially noticed in crowds of the great unwashed, and creates feelings of faintness, languor, and debility." Neuritis is encouraged by "insanitary conditions," which are depressant to the nerves. Sewer-gas entering a house may occasion persistent neuralgia, to which soap-boilers are also prone. Acrolein vapour causes headache, nausea, anorexia, and vomiting. Depressant conditions are associated with oil-boiling and varnish-making.

Habitual constipation has depressant results, especially in neurotics, and conduces, *e.g.*, to neuralgia of the breast. The ingestion of "bad food" is another factor in the production of nerve depression, while the drowsiness and languor sometimes experienced after a meal are partly due to absorption from the food of substances which have a narcotic action. There is no positive evidence that the amines, neurine, and choline in fæcal matter produce toxic conditions, and there is little evidence to show that putrescine and cadaverine are in sufficient quantities to be factors; but indol is in large amount in some cases of intestinal putrefaction, and children under these circumstances show fatigue early. Yet phenol may play a part. Skatol appears in less quantities and is less toxic than indol, but both are depressants and narcotics. Hydrogen bisulphide formed in the intestine in catarrh induces headache, vertigo, drowsiness, stupor, &c.

Residence upon damp and clay soils is depressant to the nerves, and residence upon the former, as well as in the neighbourhood of marshes, predisposes to neuralgia. Personally, I experience sometimes depressant conditions, after a shower of rain or in damp woods, which can be ascribed to volatile emanations from the soil. Residence on damp and clay soils and near to marshes predisposes to chronic rheumatism.

How far does humidity of the air induce depressant conditions by interference with the respiratory exchange?

The amines are among the substances probably concerned here with which we have not already dealt. Trimethylamine and propylamine in smaller doses are excitants; in larger, depressants. The former is used as an anodyne, and its hydrochlorate in large doses induces drowsiness and sensory paralysis. We may thus take it that, as a whole, the lower amines are depressant, when in quantity. Another group of substances are the volatile fatty acids, which are slightly narcotic and depressant. Mercaptan is a nerve depressant.

In the case of "all occupied males" the comparative mortality figure for diseases of the nervous system is greater for those employed in industrial districts than for those employed in London. This is a difficulty which must be kept in view. It is true for both periods. Of course the figure is smallest for those employed in the agricultural districts. *See* page 17.

We may recall the evidence showing that bacterial decomposition products were causative of goitre. Now cretinism is also encouraged where goitre is common. We will find that sporadic cretinism involves increased liability to certain forms of tumour.

Persons living in the neighbourhood of breweries suffer from debility and other depressant conditions, and nervous diseases are common among those working in the liquor trade. During a residence of a month (much of my time being spent indoors) upon the first floor of a building, the ground floor of which was devoted entirely to the sale of drink, I suffered from slight headache, anorexia, and lassitude, due apparently to fumes from below. The effects of chronic alcoholism are manifested in exceedingly varied forms: debility, insomnia, paralysis of sensation, loss of mental power, &c. The children of alcoholics are predisposed to nervous diseases. In acute alcoholism various stages are passed through, each of which is characterised by paralysis of definite nerve-centres. The anæsthetic effects are manifested in the insensibility to pain of drunken men. Concentrated in a vacuum, beer is said by Langer to exhibit a pronounced narcotic action similar to that of morphine; and Savory has drawn attention to the condition of habitual narcosis, due to steady drinking, among carmen driving slow and heavy waggons through the streets of London, the potent drink, I presume, being beer. Upon many beer, in small quantities even, has a soporific and depressant action. Crude spirits, *e.g.*, "Cape Smoke" and cheap Portuguese liquors, are said to produce symptoms resembling those of alkaloid poisoning, but, of course, this statement is somewhat indefinite. Alcoholic liquors act directly upon the peripheral nervous system in the mucous membranes of the mouth parts and alimentary tract; for example, their narcotic and paralytic effects upon the vaso-motor nerves in the walls of the stomach lead to hyperæmia, and their action may be so pronounced that reflex vaso-motor changes may appear in other parts of the body. Pure ethyl alcohol and the alcoholic liquors, especially the spirituous, induce peripheral neuritis and injure the nerve-cells, neuralgia being a manifestation of their effects. The sensation of burning experienced in the mouth on drinking whisky is caused by its action upon the nerve-endings. Alcoholic liquors encourage chronic rheumatism.

The alcohols are depressants—stimulants in smaller quantities—and have narcotic effects, these properties increasing with increase in molecular weight. Ethyl alcohol is used for its sedative and hypnotic action, and, of course, methyl alcohol is employed in anæsthetic mixtures. Reference has already been made to the narcotic action of the pyridine bases. Fusel oil, a complex mixture of amyl and other alcohols, pyridine bases, &c., has depressant and other effects when swallowed or its vapour inhaled. A base isolated from fusel oil, giving a different reaction to the pyridine and quinoline bases, produces general stupefaction and reduced sensibility. An acrid oil of undefined composition, obtained from raw grain spirit, has a powerful effect upon the tongue, paralysing the sensory nerves. Esters and ketones of the fatty series are depressant and narcotic, and some of the esters are used as hypnotics and sedatives. The ethers, of course, are used as anæsthetics, and aldehydes have narcotic, hypnotic, and soporific effects. Extracts of hops are narcotic, and lupulin alone is a narcotic, so also is hopein.

The incidence of diseases of the nervous system and suicide in the occupational groups considered in the earliest chapters, as well as the comparative mortality figure for "all causes," is as follows:—

Occupational Group.	Diseases of the Nervous System.		Suicide.		All Causes.	
	1890-2.	1900-2.	1890-2.	1900-2.	1890-2.	1900-2.
Chimney Sweep	95	130	36	27	1516	1240
Gasworks Service	88	61	13	10	1246	838
Indiarubber Worker, &c.	—	92	—	11	—	971
Tallow, Soap, &c., Worker	112	39	17	19	1282	689
Coach and Cab Service, &c.	94	83	23	22	1334	1062
Carman, Carter, &c.	108	81	18	17	1484	1094
Butcher	121	100	26	38	1267	1062
Fishmonger, Poulterer	108	88	23	31	1115	943
Innkeeper, Publican, &c.	186	165	36	37	1899	1669
Inn, Hotel Servant	126	110	29	37	1997	1767
Maltster	51	67	10	26	1021	734
Brewer	143	96	20	22	1649	1324
Average	112	93	22	23	1437	1114
All Occupied Males	95	78	17	19	1102	925

The inclusion of the comparative mortality figure for "all causes" needs explanation. Taken as a whole, those conditions which tend to shorten life are those which are antagonistic to the health of the nervous system, and while accidents and the results of special strains account for some proportion of the deaths in the occupational groups, the other and larger proportion is due to diseases most of which depend more or less for their development upon impaired states of the nervous system, upon a state of debility. As in some groups the number of deaths from "all causes" is so small that the comparative mortality figure for a specific disease or group of diseases cannot be held as too reliable, it is well to fall back upon a figure based upon a greater number of cases. A study of the tables will show that even this figure is not absolutely to be depended upon in the smaller occupational groups. It will be instructive to compare the comparative mortality figure for "all causes" of the occupational groups at the top of the tables with that of the groups at the bottom.

Perhaps explaining the case where cancer has supervened in the scar left by repeated blistering for neuralgia, and where keloid has followed blistering, is the fact that prolonged blistering has a local depressant effect as well as an irritative one. The caustic substances—alkaline or acid—which induce cancer or keloid may do so partly because of their effects upon the local nerve supply. Betel is a stimulant, and of course in excess must be a local depressant. Silver nitrate is used therapeutically for its effects upon the nerves. *See* page 43.

Return of cutaneous sensation after the use of blisters has been reported.

Callosities may owe their existence to lye and mineral acids.

Inflammatory conditions of the skin and mucous membranes are most liable to begin in parts where the nerve supply is impaired; and the scrofulous—the scrofulous diathesis appears to be a form of nervous debility—are prone to inflammatory states. Again, there are strong reasons for believing that it is by a trophoneurotic action, as well as sometimes by destruction of tissue-cells—even of nerve-endings—that the potent agents induce inflammation. On these grounds we may take it that on the inception of inflammatory conditions the local nerve-supply is unstable, and this instability is probably increased by the action of substances formed in the lesion—formed during the breaking down of the tissue-cells and fluids, and excreted by the bacteria. And, as has already been pointed out, this instability will be increased during the interruption of function which must exist in inflammatory lesions.

A consideration which I have had before me is the possibility that some precancerous inflammatory states are signs rather of local nerve instability than causes of the cancer by the action of their products. And in the cases of xeroderma pigmentosum and Unna's "sailor's skin" I am not inclined to give more than the slightest, if any, credit to the inflammatory products, but would rather blame the continued action of the agents which induce the inflammation, which is absent in some cases of xeroderma pigmentosum.

When bacteria attack mucous membrane, hyperæmia may manifest itself, and later, when the bacteria have multiplied, and their action is then more pronounced, the opposite condition may appear. During the earlier stages secretion may be more profuse than usual—I do not here refer to the increase in amount of fluid due to the hyperæmia—and during the later stages secretion may be practically non-existent. There may at first be hyperæsthesia, later anæsthesia; or there may be abnormal sensations—heat, cold, itching, pricking, pain. The effects may be sufficiently pronounced to produce reflex phenomena, *e.g.*, in gastric catarrh, when the nerve-endings in the walls of the stomach and the neurons of the automatic system are so strongly irritated that vaso-motor and other changes appear elsewhere. Now, I am fully aware that this is not all plain sailing ; that some of the above phenomena are in part due to destruction of the essential tissue elements ; yet, in spite of that, there is a general neurotic facies.

In septicæmia the bacterial products have depressant effects upon the nerves, the secretions may dry up and peripheral neuritis develop. When attenuated cultures of streptococcus pyogenes were injected into rabbits and guinea-pigs, they suffered from loss of hair. Rabbits inoculated with small doses of typhoid bacilli developed peripheral neuritis, hyperkeratosis, and alopecia ; and among the effects of febrile diseases are peripheral neuritis and debility. As concerns the separate substances formed, perhaps the albumoses and peptones are all that now need our attention. Injected into the veins of dogs and cats, both lower blood pressure, and have a strong narcotic action, and the albumoses, in diphtheria, receive the credit of causing peripheral neuritis.

Syphilis is a parasitic disease of which the neurotic effects are most marked : debility, peripheral neuritis, abnormal pigmentation, hyperkeratosis of the soles, &c. Gonorrhœa is also neurotic in its effects, and the toxins of the gonococcus, when injected into the blood, induce peripheral neuritis. There are grounds for suspecting that any febrile disease, leaving in its train peripheral neuritis, debility, and other neurotic conditions, may predispose to cancer and other forms of neoplasm. In a somewhat limited number of the clinical reports which I have examined, of cancer, multiple lipomata, and multiple fibroma, there was recorded a recent history of acute rheumatism, influenza, &c. Snow asserted that cancer of the breast not seldom dates from an attack of severe illness (influenza, pneumonia). After an attack of measles there developed in a boy an eruption of tumours of a doubtful nature—fibromata or angiofibromata, perhaps containing hypertrophied sebaceous glands. It is recorded that venous and lymphatic naevi of both cheeks appeared suddenly in a boy after an attack of scarlet fever. A young woman, during convalescence from variola, became paraplegic and developed multiple neuromata. *See* also pages 75, 77, and 87.

In the case of the granulomata it is conceivable that there may be a temporary paralysis of the local nervous system, an impairment of the control over growth. Not only is syphilis a cause of neuritis, but tubercle also. This is true also of leprosy ; and hyperæmia, pigmentation, hyperæsthesia, and anæsthesia are all conditions which develop in the patches preceding the formation of the nodules. In mycosis fungoides the first manifestations may be of the nature of urticaria, as well as erythematous.

In fatal and non-fatal cases of biting or stinging by insects very pronounced neurotic effects are manifested, including sometimes narcotism. Parasitic worms may induce various nervous symptoms, some of which are due to the presence in the blood of toxic excretions, and, of course, these excretions will have local effects. Their depressant effects are marked.

Statements are to be found to the effect that excessive bodily fatigue predisposes to cancer. I am unable to find corroboration in the table of occupational incidence. Of course, the excessive accumulation in the blood of substances formed during the expenditure of muscular energy induces depressant conditions, and excessive bodily fatigue is a cause of peripheral neuritis and other abnormal nervous states. These effects are in part due to failure to recuperate in face of the continued strain.

APPENDIX.

There are a number of isolated references to the appearance of neoplasms in persons who have been subjected to the action of inorganic substances which have well-defined effects upon the nervous system.

By Humphrey it was asserted that cancer developed after a course of mercury, and Prettyman suggested that slow mercurial poisoning predisposed to cancer, but we must be assured that syphilis had not been under treatment in the cases which gave origin to these remarks. However, it is not impossible that mercurial treatment superadds its effects to those of the syphilitic toxins. Dennis mentioned a case where cancer was due to the irritation of a false palate made of red rubber, and the action of sulphuret of mercury, dissolved out by the saliva, was suggested. Of course, in this case tangible reasons are absent for giving credit to anything more than the mechanical irritation.

Stanwell had under his charge cases of epithelioma where extensive treatment with pure phosphorus in the form of perles, or pills, had been undergone at earlier periods of life, and the opinion was hazarded that phosphorus may be a cause of cancer.

Hutchinson recalled cases in which multiple warts on the hands were supposed to have originated from prolonged contact with iodine and preparations of iodine among persons engaged in the photographic industry. Now potassium iodide is used in syphilis, and suspicion may therefore be directed towards it as a possible agent in increasing the incidence of cancer among persons suffering from that disease, in addition to its effects upon the mouth.

Morny and Malloizel reported the occurrence of multiple telangiectases in a painter suffering from lead-poisoning. The telangiectases were symmetrical, and seemed to correspond with nerve areas. Yet there is little in the tables of occupational incidence to justify even the suspicion that lead-poisoning is a factor in the causation of cancer.

CHAPTER XVII.

THE RELATIONSHIP BETWEEN NAEVI AND THE NERVOUS SYSTEM.

THE proof of the neurotic basis of abnormal pigmentation of the skin, hyperkeratosis, abnormal conditions of the hair, and telangiectases, may be taken as part proof of the neurotic basis of naevi ; so also may the proof of the neurotic basis of hypertrophy, for naevi seem frequently to be associated with hypertrophied conditions. In addition to evidence upon the latter point, there is a good deal of evidence further associating naevi with the nervous system, and it may well be brought together to serve as a preliminary to similar evidence for other neoplasms.

Vascular naevi may be associated with hemihypertrophy of the limbs—one of the stigmata of degeneracy—sometimes accompanied by other signs of nervous derangement. They are often associated with macrodactyly.

Klippel and Trenaunay described a disease under the name of "varicose naevus with osseous hypertrophy." This disease was said to be characterised by three dominant symptoms : (1) vascular naevus with metameric distribution extending over the whole of one of the lower limbs ; (2) varices limited exclusively to the affected side, and dating from birth or early infancy ; (3) hypertrophy of the tissues on the same side, involving mainly the bones. The disease is limited by the middle line of the body, and the regions of skin affected by the naevi correspond to the peripheral distribution of one or more spinal nerves. Sensation may be altered in the skin over the naevi, but it may be normal, while the hair may be deficient, increased in amount, or arranged in tufts. In one case there was continuous salivation, in another continuous lachrymation, in yet another the secretion of the sebaceous and sudoriparous glands was extremely profuse. Other trophic abnormalities appear. Klippel and Trenaunay uphold the theory, advanced by Reverdin and others, that the disease is due to an infective agent acting upon the vascular system of the fœtus.

Johnston and Fowler recorded the case of a baby girl with numerous telangiectases, or "capillary naevi," on both sides of the body ; those on the right side of the forehead were sharply limited by the middle line. The right side of the body was hypertrophied. Noting that capillary naevi, or larger telangiectases, are relatively common in cases of hemihypertrophy, it is remarked that sometimes they are only temporary, appearing when the patient is excited. Attention was drawn to the fact that Hornstein in one case found changes in the peripheral nervous system.

Exhibited by Little, a girl had a vascular naevus distributed over the whole of the right side of the body, and the right arm and leg were larger than those opposite. Adams reported a case of hypertrophy of the right leg in a youth who had a vascular naevus on the same leg extending over the scrotum and stopping in the middle line.

In these two cases there is a possibility that the hypertrophy was due to the extension of the vascular tumour throughout the whole of the limbs.

Extensive naevi are usually also hairy, and are sometimes symmetrical, when they show a predilection for the bathing-drawers region. Sometimes they are unilateral, corresponding more or less accurately with the territory of a cutaneous nerve or group of nerves. In one case a hairy mole occupied the entire half of the face, and vascular naevi frequently cover the larger part of one half of the face, and in some cases even one half of the body. Large unilateral naevi sometimes pass the middle line of the back, and it is curious that the spinal nerves also overlap the middle line. When large hairy naevi appear upon the trunk, the hairy part is sometimes very sensitive.

Seven cases of naevus—one pigmented, two pigmented and warty, one pigmented and hairy, and three vascular—reported upon by Etienne, showed clearly a nervous distribution.

Cheatle records a remarkable case of vascular naevus mapping out the area of distribution of the third cervical nerve of one side even to the very notch in its lower border.

An interesting case of extensive naevus has been shown by Evans. It was especially marked upon the left side, and involved the upper limb and the chest, where the mesial border was well defined. On the left side it affected the palmar aspect of the hand and also the dorsal aspect of the terminal phalanx of the fingers. Now this portion of the back of the fingers is supplied by the palmar and not by the dorsal nerves, as Evans pointed out.

Philippson, Petersen, and Galewsky have called attention to the relationship between the distribution of naevi and the lines of Voigt, *i.e.*, zones between the spheres of action of two neighbouring cutaneous nerves. Some cases support this generalisation.

Naevi sometimes occur at Head's "maximum points" in the peripheral distribution of posterior spinal ganglia, *i.e.*, the foci within the areas of referred pain in visceral disease at which the pain is most acute. These foci correspond somewhat closely to the points at which the nerves come to the surface.

Naevus unius lateris (von Bärensprung), neuropathic naevus (Simon), neuropathic papillomata (Gerhardt), are multiple, pigmented, flat, or warty growths, the distribution of which often corresponds to the region of particular cutaneous nerves—the trigeminal, or one or more spinal nerves—and when unilateral, as they generally are, they cease in the middle line of the body. They may be arranged upon the trunk or extremities on the plan of an eruption of herpes, and are frequently seen with cutaneous and other neurofibromata. In cases described by Neumann one entire half of the body was darkly pigmented and partly covered with these growths. By von Recklinghausen and others it was suggested that they are due to an intra-uterine neuritis or myelitis, which so lessens the control of the nutrition of the skin that certain elements hypertrophy. It was assumed by von Bärensprung that they depended upon an intra-uterine affection of the spinal ganglia. Commenting upon Neumann's cases, Ziemssen pointed out that we must look to a more central part of the nervous system than the spinal ganglia. In his remarks upon a case, exhibited by Mackenzie, of unilateral papillary growths which may have been naevi, Hutchinson suggested that they were possibly due to intra-uterine herpes.

Campana, with a record of fifty cases of naevus, in which their distribution showed unmistakably their relation to the nervous system, considered that intra-uterine changes should be looked for in the peripheral branches and not in the nerve-centres. While this position may be tenable in the case of small, isolated naevi, it cannot be held, for example, in some cases of naevus described in the last paragraph.

It was asserted by Etienne that an hypothesis of intra-uterine peripheral neuritis, depending possibly upon a comparatively slight infectious illness of the mother (influenza, tonsillitis, &c.), or upon a fœtal toxæmia (arising from maternal gastric and intestinal conditions), would explain a large number of cases of naevi.

Little has exhibited a case of unilateral naevus unius lateris, in which a pigmented and partly verrucose streak extended from the pubic arch along the inner side of the thigh and leg to the instep on the right side. The upper part of the streak extended on to the inner side of the scrotum exactly in the position of the small scrotal flap assigned to the second lumbar by Head. The streak seemed to correspond to the distribution of the second, third, and fourth lumbar segments as mapped by Head.

In Meissner's case of unilateral naevus verrucosus of the left side, hearing on that side was deficient. The patient masticated upon the right side, and the musculature of the left side was less developed than on the right. Meissner saw in the histological data a proof of vaso-motor disturbance, and, with other evidence in view, pronounced in favour of a neural etiological factor in the causation of naevus verrucosus, possibly some lesion of the medulla oblongata.

In Taylor's case of unilateral naevus verrucosus associated with certain abnormalities of pigmentation, the patient sweated more freely upon the right side, the side affected. There was alternation of deeply pigmented papillomata with pigmented patches of skin, and the merging of this pigmentation into decolourised patches, perhaps comparable with the white moles of Hutchinson. The distribution was in the track of certain nerves. This case and that of Meissner are evidently cases of naevus unius lateris.

Bergmann has asserted that pigmented naevi are always associated with a thickening of the sheaths of the cutaneous nerves. It may be said that nerve fibres have been traced into pigmented naevi.

Evidence showing a relationship between neurotic conditions and the abundant occurrence of naevi is more liable to sources of error—depending, as it does, largely upon personal judgments—than evidence of a nervous distribution, but it seems to be generally accepted.

Epileptics, idiots, and hydrocephalics are reported to be particularly liable to pigmented naevi, and von Harlingen asserted that they are found more frequently in the insane than in normal individuals. Ashby and Wright remark that naevus lipomatodes appears to be associated with idiocy, and they figure an idiot with a pigmented and hairy naevus lipomatodes occupying the bathing-drawers region. Pigmented naevi occur not infrequently in cases of myxodœma, a disease in which the nervous system is early affected. Both pigmented and vascular naevi are among the stigmata of degeneracy, and it has otherwise been noted that there is a marked liability to pigmented naevi among persons who have some gross deformity, such as hare-lip or cleft palate.

Little has exhibited a child, who, when at the age of three, had a severe "fit," which was followed by paralysis of the right leg. Three weeks later there appeared upon the left side of the chest an eruption of naevi which had persisted unchanged up to the time of exhibition at the age of six. Numbering about forty or fifty, they were grouped in a manner absolutely like herpes zoster, and their position was comparable with the innervation of the third dorsal segment.

The occasional spontaneous retrogression of vascular naevi is perhaps explicable by a return to normality of the nerves concerned in the supply of the part. And their cure by concentrated arc-light and by the action of radium, which affect the nervous system, is significant. Telangiectactic naevi have been cured with the actinic rays, and vascular, pigmented, and hairy naevi with the X-rays. The retrogression of vascular naevi after attacks of febrile disease may be consequent upon changes in the nervous system.

In a case where four vascular naevi were present in a young child, one was cured by plunging red-hot needles through it, when two of the others spontaneously disappeared. Croly, whose case this was, made the suggestion that the operation affected the sympathetic nerve-supply of the two naevi spontaneously cured.

I may conclude by recalling the fact that a pigmented mole is frequently found in place of the dorsal tuft of hair in spina bifida occulta.

CHAPTER XVIII.

THE NERVOUS DISTRIBUTION OF NEOPLASMS.

IN the chapter upon naevi a relationship was shown to the distribution of nerves. A similar relationship can be proved in the case of other neoplasms.

Cheatle has given us, in a series of communications, the results of some important observations upon the relation between cutaneous areas of nerve distribution on the one hand, and, on the other, the points of origin in the skin of cancer (squamous epithelioma, rodent ulcer, Paget's disease) and the areas over which it spreads.

He found that the incidence of squamous epithelioma and rodent ulcer upon the head and face is very closely associated with the distribution of the trigeminal nerve, and that when rodent ulcer is multiple, the points of incidence nearly always fall within the area or areas of one or both trigeminals respectively, and chiefly on those parts which are not overlapped by the second cervical spinal nerves.

In his earliest paper he pointed out, in the case of the trunk more particularly, that the incidence of cancer frequently falls upon Head's " maximum points " in the peripheral distribution of posterior spinal ganglia. In cancer of the hand the commonest point of incidence is over one of the " maximum points," and he has observed at the same place on the backs of the hands of old people warts and superficial blackish-yellow patches. Head's experiment upon himself was referred to : segments of his radial and two branches of his external cutaneous nerves were excised, when sensation was lost for tactile, pain and temperature impressions in the skin of the area which the nerve supplied ; eventually a trophic ulcer developed over this particular " maximum point." In one of his later papers, noting that he had previously been without sufficient data respecting the face, he was able to show that rodent ulcers there appeared most commonly at the " maximum points."

Dealing with the spread of the growths, or, to speak more correctly, the extension of the process of transformation of previously normal epithelium into a riotous form, cases were described and figured where the process of extension was limited at the boundary of a nerve territory. A case of Paget's disease began at the " maximum point " in the territory of the eleventh dorsal posterior spinal root ganglion of the left side, and extended forwards and backwards, ultimately assuming a zoster-like distribution. The anterior and inferior edges of certain cases of rodent ulcer corresponded to the anterior and inferior limits of the skin supplied by the great auricular nerve, which is itself included in the supply of the second cervical posterior spinal root ganglion. The anterior edges corresponded also to the anterior edge of an area of tactual anæsthesia in a case where the second and third cervical posterior spinal root ganglia were removed. Cheatle had a case of naevus with the same boundary. This arrest of rodent ulcer is temporary only, and when it spreads into nerve territories adjacent to the territory in which it begins, it follows the course of distribution of these nerves. If these adjacent territories are rendered anæsthetic by the destruction of their nerves, the growth does not extend into them, at least temporarily. In cases of cancer of the tongue he noted that occasionally there is a limitation in extension at the middle line, and that the tip, which has a different innervation to the remainder, may escape. Having noticed how squamous epitheliomata which develop upon scars have their extension limited at the edges, he tested the tactile, pain and temperature sensations of many scars, and found marked abnormality in most of them. Cheatle also showed that rodent ulcer, when spreading, tended to map out certain cutaneous muscles, and the probable importance of this fact is mentioned because it is not yet known what is the exact nervous relationship between the cutaneous muscles and the skin of which they are component parts.

In one of his papers Cheatle was able to strengthen his work by proving that the points of incidence of rodent ulcer on the face and trunk are common to the points of incidence of the so-called neurotrophic diseases leucoderma and scleroderma, and that the points of incidence of these two diseases correspond to points at which cutaneous nerves come to the surface ; further, that the spread of rodent ulcer upon the head, face, and trunk appears, on the whole, to resemble the spread of leucoderma and scleroderma.

Cheatle indicated in his first paper that the spread of cancer in the skin was associated with degenerative changes in the posterior spinal root ganglia which supplied the area invaded. In a later paper he recorded that in a case of rodent ulcer beginning at the left side of the face and extending to the right side, similar degenerative (intracellular) changes were found in the right Gasserian ganglion, and that in the left Gasserian ganglion were manifested inflammatory conditions. In the case of Paget's disease which appeared upon the left side of the trunk and assumed a zoster-like distribution, while squamous epithelioma appeared upon the hip of the same side, inflammatory changes were found in the posterior spinal root ganglia of the nerves supplying the two areas in which the cancerous growths began, and the disease being confined to these areas, the neighbouring ganglia were therefore normal. There is a very strong presumption that the inflammatory changes were primary to the cancerous growths, and the degenerative secondary to the invasion. Elsewhere it is suggested that if more than one " maximum point " is affected in the same nerve area, the cause is probably central ; if only one, the cause is probably peripheral.

The position taken up by Cheatle, in view of the above-mentioned facts, is as follows : " I only wish to point out that the breakdown of the cell or cells into carcinoma may possibly be due to some direct or indirect nervous or trophic influence over the area in which it occurs."

Walsh has exhibited a case where nodules, for the most part confluent, appeared in the form of an extensive sheet upon the left side of the chest and in scattered areas elsewhere. The eruption began in the cutaneous supply area of the fifth dorsal ganglion, and developed later in the territories supplied by neighbouring cervical and dorsal ganglia. In the earlier stages the eruption was so characteristic of nerve implication that it was actually mistaken by a medical man for intercostal herpes zoster. On microscopical examination it proved to be lenticular scirrhus.

To add to the evidence already given of the distribution of naevi in nerve territories, I have so far been unable to collect many similar facts bearing upon other forms of innocent tumours, though there are numerous accounts of multiple tumours containing details strongly suggestive of something of the kind.

Whitfield has shown a case of multiple myoma cutis (leiomyomata), preceded by blisters, in which the tumours existed upon the right side of the forehead. The affected area corresponded almost exactly with that of the external branch of the right supraorbital nerve, though the tumours did not extend backwards into the hair as far as this branch was distributed. In a case of Beatty's, a group of multiple leiomyomata of the skin appeared upon the left side of the forehead, and went no further than the middle line. Similar tumours on the upper part of the thorax were bilateral and symmetrical. Hardaway reported a case of multiple leiomyomata of the skin, which nearly all appeared upon the back on the right side, and were distributed in nerve tracts. He could not find any nerves in them. Roberts, in a case of leiomyomata, suggested that they had originated from the arrectores pilorum, but did not assert that he had found a distribution in nerve territories. The chief points in the clinical history were : (1) shooting pains felt during cold, damp weather ; (2) the unilateral distribution of the tumours, the left side of the face being quite sound ; (3) hypertrophy of colourless lanugo hairs in the immediate neighbourhood of the tumours, the other portions of the face being quite hairless. As against the above evidence it must be noted that in most of the cases of leiomyomata of the skin there has not been noticed a nervous distribution, yet it is only in recent years that attention has been paid to this point.

It has been shown by von Recklinghausen that many vascular and lymph angiomata are distributed in nerve territories.

Neurofibromata—including under this term molluscum fibrosum—as will be pointed out later, may be distributed in nerve territories.

Cheatle has mentioned that diffuse papillomata of the tongue may show middle line limitations.

A case of multiple keloids has been exhibited by Mackenzie which extended as a zonular band around the right side of the chest from the spine to the sternum. It was doubtful whether they arose secondarily in the seat of herpes zoster, or were primarily due to a lesion of the nervous system in the posterior roots of the spinal nerves. There is a strong presumption that the first explanation was the true one, but it may be significant that the whole of the herpetic lesions took on keloid action. The patient had a tendency to keloids, for they had developed also where he had been bitten by a centipede.

Xanthoma multiplex is a form of growth which some consider to be merely an expression of a low inflammatory state. It is frequently associated with megrim or other neuralgiæ, and is encouraged by nervous fatigue. Hereditary cases are frequently unilateral, and Hardaway has found a zoster-like distribution. Xanthoma is one of the stigmata of degeneracy.

On pages 74 and 92 is some additional evidence.

A symmetrical distribution of neoplasms has been ascribed to the condition of the blood; but should this rather not be looked upon as an active cause producing its effect upon the nervous system ? How otherwise can their symmetry be explained than as a result of nerve derangement, except in those cases where the existence of symmetrical precancerous inflammatory lesions has been proved or can be surmised ? And even these cases do not form an insurmountable obstacle. It may be urged that the symmetry of neoplasms is far from being the rule, yet this applies also to trophoneurotic inflammatory conditions of the skin and to abnormal states of cutaneous sensation. But while the condition of the blood, say the presence in it of a toxic substance, may affect symmetrical nerves directly, the work of Cheatle opens the question of the responsibility of symmetrical ganglionic inflammation, whether or not the latter is due to a blood condition.

The symmetrical development of cancer has been reported on the limbs and the auricles of the ears, and in the eyes, testes, ovaries, and breasts. In some cases of sarcoma idiopathicum multiplex hæmorrhagicum the growths are symmetrically distributed. Exostoses, cutaneous neurofibromata (molluscum fibrosum), and lipomata may be symmetrical, and in one case a lipoma in the middle line of the breast was bilobular. Adenoma sebaceum is usually symmetrical, and this is sometimes the case with angiokeratomata, naevi, telangiectases, and xanthoma multiplex.

When numerous multiple tumours are confined to one side of the body, and are extensively distributed on that side, we can readily believe that they have a neurotic basis.

CHAPTER XIX.

Nerve Instability and Neoplastic Tendencies.

WHILE I will now endeavour to show that neurotic tendencies predispose to both cancerous and innocent growths, it must not thereby be understood that these tendencies are always present, even in a subtle form which cannot, in the present state of our knowledge, be detected, for agents acting under favourable conditions may derange the most perfectly-balanced nervous system.

Cancer.

That insanity, imbecility, epilepsy, and other unstable conditions of the nerves run in families along with a tendency to cancer may now be taken as proven. Lancereaux also has it that the neuropathic temperament predisposes to the development of epithelioma. Sabathier claimed that hypochondriacs are more exposed to cancer, while seventy years ago Hodgkin remarked that individuals of the melancholic temperament were said to be the most liable to melanosis (malignant). At the outset we are faced with the objection that cancer is rare among the insane and is practically unknown among idiots and imbeciles. But this is not surprising when we remember that the latter seldom reach the cancerous ages, dying mostly in childhood and youth, while there is a high mortality among the insane, the death-rate before middle age being pronounced. Relative freedom from the attack of the causative agents which have been considered in previous chapters can be a small factor only in reducing the incidence.

Beneke remarked that cancer patients are peculiar constitutionally by seldom possessing a sanguine temperament, being, on the contrary, remarkable for a lymphatic temperament and for defective mental and physical energy.

That tuberculosis and cancer run together in families may also be taken as proven. It has a number of times been remarked how frequently the surviving member of a tuberculous family dies of cancer. Statistics show that the death-rate from cancer is high among cases of healed tuberculosis, while autopsies of cancer patients prove a greater frequency than normal of old tubercular lesions. Now, tuberculosis tends to appear in neurotic families, and many admit the existence of a debilitated state of the nerves which predisposes to tuberculosis. The insane, epileptics, and the paralysed somewhat frequently give birth to scrofulous children, while idiots have scrofulous tendencies. I have considered the so-called predisposing agents of tuberculosis, and find that all are neurotic in effect and debilitating, and to remove debility is perhaps the most efficient method of combatting tuberculosis. To prove the neurotic basis of tuberculosis is to strengthen the case for the neurotic basis of cancer, but the objection will be made that the two diseases seldom occur at the same time in the same individual, and they appear to be antagonistic in some respects. Cancer does not usually develop in a tubercular individual until the tubercle has healed, and mammary cancer at least has been noticed to retrograde upon an acute outbreak of pulmonary tubercle. In a later chapter it will be made clear that this antagonism is that usually manifested between cancer and febrile diseases, and is dependent upon a change in reaction of the blood-serum. Quite a different point is involved to the neurotic predisposition to both diseases.

As tuberculosis is one of the causes of neuritis, it may be that this is one of the reasons why the incidence of cancer is higher in cases of healed tuberculosis.

Arthritism and cancer, and herpetism and cancer, appear also to have affinities. The occurrence of twins in a family is claimed to be a sign of its neurotic tendency, and in a family in which were several cases of twins, Critzmann found that the non-twins were cancerous. Féré, in a similar family, the twins being neuropaths, found cancer among several of the non-twins. Behla has blamed marriage between near relations as a predisposing cause, and Hutchinson found that the children of parents more advanced in years were more exposed to attack by cancer. By Manichow a considerable number of cases were reported in a district where consanguineous marriages were frequent.

Williams often observed obesity in cancer patients.

Innocent Growths.

There is quite an accumulation of evidence associating innocent growths with neurotic states, neuropathological conditions, the scrofulous diathesis, hypertrophied and other teratological conditions, and so on.

Among the anatomical stigmata of degeneracy, in addition to pigmented and vascular naevi, are adipose thickening of the skin, xanthoma, and neurofibromata, including molluscum fibrosum. Some remarkable examples of neurofibromata are found in cretins and idiots.

Lipomata, exostoses, and diverse tumours of the skin, are found along with congenital malformations in individuals suffering from mental and nervous affections.

In cretinoid idiocy the skin may be the seat of numerous fatty tumours, and well-developed lipomata are seen in most cases on each side of the neck and occasionally in the armpits. Multiple lipomata, frequently symmetrical, are so often associated with neurotic conditions and with arthritism that Beck considered that they are the manifestation of a trophoneurosis. Lipomata coincide sometimes with teratological conditions, occurring within the seat of the latter or elsewhere. Targlowa recorded a case where symmetrical lipomata, seven pairs, developed in a man affected with general paralysis. Somewhat similar cases have been reported by others, and lipomata have also been found in tabes. Madelung observed the growth of fatty tumours at the insertion of the deltoid muscle, following upon neuralgia and tremors due to contusion, and Matthieu described a case in which sciatic neuralgia was attended by lipomata upon the leg. As observed by Buchterkirch and Bumke, multiple, symmetrical lipomata followed a contusion of the spinal chord. Adiposis dolorosa, which is, perhaps, merely a form of ordinary lipomatosis, affects women who frequently are neurotic or addicted to alcoholism. It may be symmetrical and accompanied by pigmentation of the skin. There is diminution of cutaneous sensation, paræsthesia, and a sense of coldness in the parts affected. Degenerative changes have been found in the nerves supplying the affected areas. It will now be seen how strong is the basis of fact for the theory, advanced by some, that lipomata owe their origin to a trophic disturbance of neuropathic origin. Some of these putative lipomata may not be tumours in a strict sense, but I find myself unable to draw a line between the true and the false.

Those who suffer from von Recklinghausen's disease are frequently neurotics, or display some malformation or other sign of degeneracy. The following are the characteristics of this disease in cases where it is completely developed: (1) multiple neurofibromata of the skin (molluscum fibrosum); (2) multiple neurofibromata proper; (3) increased pigmentation of the skin, freckle-like or in large patches. The distinction between the two first symptoms depends merely upon whether or not the tumours are located in the skin. In exceptional cases the tumours and pigmented areas follow the distribution of one or more cutaneous nerves, and when the molluscous tumours are unilateral, they may stop exactly in the middle line, even when in the diffuse form of pachydermatocœle. Nerves could not be found by von Recklinghausen in some of the molluscous tumours examined, and he suggested that they had degenerated. A large number of cases are congenital, and in the remainder mental anxiety, infection, overwork, mechanical traumata, cold and bad hygienic surroundings are some of the causes receiving blame. It is suggested by von Recklinghausen that the tumours occur most frequently in spots where pressure and friction of the clothing is to be expected. This disease is hereditary.

Ross has it that the phthisical and scrofulous seem to have a special liability to neuromata.

A very large proportion of patients suffering from adenoma sebaceum—a term applied to more than one kind of tumour containing an hypertrophied sebaceous gland—are neurotics (idiots, epileptics, hystero-epileptics). The epidermis over the tumours is pigmented and may be warty, and in most cases there are telangiectases over and around them. They may be symmetrical, and usually co-existing with them are pigmented and vascular naevi, warts, and fibromata.

Hard fibro-adenomata of the breast—sometimes attributed to blows, squeezes, and lacteal irritation—is often associated with the hysterical temperament, and is most common in women of irritable and delicate nature. It is said to be often connected with, if not dependent upon, uterine irritation and sexual excitement of an irregular kind (meaning, I suppose, onanism).

In young persons who are constitutionally delicate, warts are thrown out in crops like an exanthema, and they are said then to yield to a treatment directed towards the improvement of the nervous system as well as of nutrition. Tilbury and Fox remark that certain ill-conditioned subjects seem to have a tendency to warts. In elderly persons a warty state of the skin is sometimes associated with a tendency towards asthenic ulceration. Warty growths are not infrequent in myxodœma, and it has been said that warts tend to appear in the scrofulous. I would suggest that when "seed warts" develop around a spot from which a wart has been removed, the irritation incidental to removal has affected the local nerve-supply and caused the formation of the warts, there being a predisposition to their formation.

Mc.Call Anderson believed that warts were remotely connected with the scrofulous diathesis.

Angiokeratomata develop upon the basis of chilblains, which are liable to occur in neurotics. After repeated temporary dilatations of small blood-vessels, telangiectases develop, and later the skin becomes warty. Because the patients show various signs of disordered peripheral circulation, that is not to say the angiokeratomata are due merely to vaso-motor disturbance, as is suggested; we must look towards a general disturbance of the local nerve-supply, part of which only is apparent. Some of the patients are tubercular, and there are observers who would say the same of the growths. Vidal has shown that a condition practically similar to angiokeratomata may follow an attack of urticaria. Naevus verrucosus, a neoplasm also strongly resembling it, like other naevi sometimes follows the course of distribution of nerves.

Ichthyosis has a well-defined neurotic basis, and the warty form—ichthyosis hystrix—is sometimes associated with mental weakness. But it seems to be generally accepted that ichthyosis hystrix is identical with naevus unius lateris.

In chorea there is sometimes a warty condition of the knuckles of which I cannot yet find details.

Pospelow noted the frequency of keloid formations among the trophic affections of the skin in syringomelia; others were vasomotor phenomena, and alterations in growth of the hair and in sweat-secretion. It has been suggested that the strumous are more liable to keloid.

It is noted by Sutton that individuals with multiple chondromata often manifest rachitic tendencies. From a study of the predisposing agents and nature of rickets, I make out that it has a decidedly neurotic basis.

Macroglossia, a form of lymphangioma, sometimes unilateral, is not infrequently found in cretins, and is usually associated with imbecility and developmental errors. In cretins is also often found a similar condition of the lips.

Hypertrophy of the gums, frequently congenital, may be associated with nervous deficiency and with the scrofulous diathesis. Some of the patients are dwarfs. It may be unilateral, and is sometimes accompanied by other developmental errors, mostly hemihypertrophic. It may be that some are examples of general hypertrophy of the gum tissues; most, if not all, are vascular naevi or lymphangiomata and co-exist with pigmented or vascular naevi in other parts. The surface of the growth is sometimes covered by hypertrophied papillæ. Three cases in a family were reported by Murray: a girl, shy, not unintelligent, deaf at times, had also molluscous tumours, and on each tibia small exostoses. The ends of certain fingers, the thumbs, and toes were hypertrophied. Her brother, of somewhat feeble intellect, had also the end of a finger hypertrophied and a molluscous tumour on the back of another. Her sister, slightly rachitic, intelligent, showed three molluscous tumours. The parents were cousins, and enjoyed average health, but the mother had always been very nervous, had suffered from mental depression until her first child was born, and was the subject of habitual constipation. Her mother died of consumption, but her father was long-lived. The three children were born and reared under unfavourable hygienic conditions, the sleeping apartment being so damp that the mattress was mouldy. An older child than these, born under more favourable conditions before removal of the family to this residence, and a younger child, born after removal from it, were healthy and normal, except that the younger had vascular naevi on the side of the face. Humphrey, in 1886, described a unilateral case in a girl, healthy and intelligent, the hairs of whose eyebrows on the affected side were coarser, more numerous, and covered a larger area. There were other signs of asymmetry, while hairless, pigmented naevi and some deformities were also present. The ten cases then known were recalled: (1) feeble intellect, stunted development, ill-shaped head, large abdomen; (2) epileptic, unusual quantity of hair from birth on head, arms, and legs; (3, 4, and 5) Murray's cases just described; (6) apparently healthy;

(7) epileptic ; (8) apparently healthy ; (9) average mental capacity, never in good health ; (10) feeble intellect, covered with a remarkable hairy growth, exhibited as a " bear woman."

Subcutaneous angiomata, which are sometimes multiple and are hereditary, coincide sometimes with other anomalies, especially with hare-lip. Cavernous angiomata and lymphangiectases occur not infrequently with hemihypertrophy, and venous and lymphatic troubles predominate, which are limited to the affected side ; these abnormalities cease at the middle line of the face, neck, scrotum, &c. There is a tendency for conditions of hypertrophy and atrophy and other developmental errors to appear upon the same side of the body as unilaterally-distributed tumours.

An interesting case was described by England of multiple neurofibromata accompanying hemihypertrophy of the left side in a mentally-backward child. The hair of the left eyebrow was coarser and more abundant than that of the right, and the hair of the left side of the body coarser and less inclined to curl than that of the other side. The left side of the face did not perspire as much as the right, and felt colder.

Acromegaly is frequently accompanied by cutaneous neurofibromata (molluscum fibrosum), and an abundant formation of warts has been observed in some cases. The sweat glands are sometimes hypertrophied, and the sebaceous glands are often prominent.

Sternberg, among the types of giant which he distinguishes, mentioned one type showing exostose-like tumours, and another with tumour of the scrotum in childhood.

The inheritance of cancer and other forms of neoplasm (sarcomata, lipomata, myomata, chondromata, exostoses, neurofibromata, uterine fibroids, ovarian cysts and papillomata, angiomata, naevi, warts, angiokeratomata, &c.), is a fact corroboratory of the neurotic hypothesis, for the inheritance of neurotic conditions is undoubted. Xeroderma pigmentosum frequently occurs among brothers and sisters.

In the above notes I have taken the line that the innocent tumours are effects of neurotic conditions, but in some few cases the latter are due to the presence of tumours in the cranium. The most familiar example is the association of epilepsy with a vascular tumour of the dura mater.

CHAPTER XX.

Miscellanea upon the Neurotic Hypothesis.

THIS chapter will be devoted to miscellaneous facts and suggestions bearing upon the neurotic hypothesis which do not come within the scope of previous chapters.

Young determined the presence of nerves in sarcoma, but the peripheral branches were not evident. Vaso-motor nerves must have been present for the supply of the blood-vessels, but more than this could not be asserted. He would not say that nerves apparent in sections of carcinomatous growths were constituent parts of the tumour, and rather believed that they represented nerves of the normal tissues invaded by the cancer cells.

In sarcoma idiopathicum multiplex hæmorrhagicum Semenow and others have found changes in the nervous system, chiefly in the spinal ganglia, and it is suggested that the sarcomatous lesions are due to a paralytic angioneurosis, which may be looked upon as an impossible explanation. Mackenzie asserted that this disease mostly occurred in those subjected to fatigue and hardship, and it is significant that some few cases have been cured by administration of arsenic.

By Charcot it was shown that the joint complications of tabes with osteophytic growths are the result of atrophy of the large anterior cells of the spinal chord.

Attention has already been directed towards the observations of Hardaway upon leiomyomata, von Recklinghausen upon molluscum fibrosum, Hornstein upon telangiectases with hypertrophy, and Bergmann upon naevi, with respect to the nerve supply, and to the nerve changes in adiposis dolorosa.

Mantegazza observed hypertrophy of the connective tissue, and of the periosteum, bones, and lymphatic glands, after experimental section of nerves in animals. And division of the large nerve-trunks in man, especially those of the extremities, is not infrequently followed by circumscribed hyperplastic phenomena in certain parts (skin, hair, bones, and joints) side by side with atrophy of other parts (muscles and subcutaneous tissue). Hypertrophy of the face and ear after section of nerves has already been mentioned.

In an address upon the trophic functions of nerves, Gaule mentioned an experiment in which a knife was plunged into the second spinal ganglion of a frog. In the skin appeared abnormal pigmentation and atrophy along with warty growths.

In paralysed limbs the skin may become hypertrophied.

The abnormal growth of the cock's spur in Hunter's famous experiment may have been due to its removal from the zone of control of its proper nerve-supply, the abundant blood-supply being only a secondary factor. And when masses of tissue-cells—becoming displaced from their parent tissues during fœtal life, or later as a result of injuries (implantation cysts), or perhaps as a result of destructive processes around them, such as appears to happen at the edges of ulcers—take on abnormal growth, this may only be possible because they are not under nervous control, though they may have to wait for impairment of the resisting powers of the connective tissue, and maybe also, in the case of malignant tumours, for a change in the reaction of the blood ; there does not seem to be any evidence of the reaction of the blood in the case of innocent tumours. It would appear that hyperalkalinity of the blood-serum is a characteristic feature in cases of malignancy.

Campana believed that sarcoma cutis is intimately related to the nervous system. This affection is commonly associated with sarcoma and fibroma of the peripheral nerves, which often antedate it, and the nerves have a considerable influence in its spreading and development. In one form the sarcoma cutis had appeared symmetrically, like an exanthema, in the manner of various erythemata which are accepted as of nervous origin, and which frequently correspond to the peripheral distribution of nerves. Campana bases his case partly upon the frequent occurrence of recurrent nettle-rash or itching in the extremities preceding the sarcoma, but in one case the itching followed, and I would like to be assured that it is not merely the result of abnormal proliferation of cells around the nerve terminations. Mc.Call Anderson asserted that chronic pruritis, of many years' duration, of the anus and vulva is often followed by epithelioma, but the frequent mechanical irritation by the patient must be remembered.

Assertion has been made that scars, especially of burns and scalds, are very liable to epitheliomatous degeneration, a general statement which must be taken for what it is worth. Sensory organs are usually below the normal number in scars, yet scars are sometimes hypersensitive, while they may be the seats of abnormal sensation (itching, burning, &c.). Regenerating nerves make their way with difficulty through the compact fibrous tissue of scars, which are predisposed to neuralgia. But two other explanations of the greater liability must be kept in view : scars are prone to inflammatory conditions ; and, owing to their insensitiveness, mechanical irritation cannot be readily appreciated and provided against. I have already mentioned Cheatle's experiments upon scars, attempted with another purpose in view.

The increase in the incidence of cancer with the approach of old age appears to have more than one causative factor, but one is probably neurotic. The onset of tissue degeneration in old age is common to all of the tissues, but it is manifest that if the nerves take an equal share only in this degeneration, a breakdown in trophic function is then more liable to occur than during the earlier periods of life. The nervous breakdown is manifested in abnormal pigmentation of the skin and abnormal conditions of the hair, in a tendency to the development of telangiectases and of hyperkeratinisation, and in many general neurotic conditions.

There is a tendency for the age period of incidence of certain kinds of neoplasm to be demarcated by the age of puberty in both sexes, and by the menopause in women. It may be possible to correlate this with the partial reorganisation of the nervous system at these periods, when numerous signs of nervous instability are manifested. Of course, special forms of traumata, operative before or after these periods, will have to be accounted for. If it is true that cancer occurs in the young mostly in organs which early lose their functional activity and undergo some degree of degeneration, instability during the necessary reorganisation of the nerve-supply may be partly responsible, and this may apply also in the case of women to the breasts and uterus.

The retrogression of uterine fibromyomata at the menopause may therefore have its significance.

When the breakdown of normal epithelium into cancerous tissue extends centrifugally over the skin from the point of its first appearance, failure of the nerves extending centrifugally may be the cause. And when carcinoma becomes annular in a tubular structure, say the œsophagus, the method of spreading may possibly be correlated with the distribution of the nerves.

Hypochlorhydria is found in neurasthenia, hysteria, and tabes, and in febrile diseases, and in the course of the latter the blood-serum is less alkaline than normal, while they also have neurotic effects. It would therefore be nearer the mark to suggest that the hypochlorhydria of cancer is due to failure of the nerves to stimulate the glands concerned than to ascribe it to a hyperalkaline blood-serum. This nerve failure may have its significance.

The cure or improvement of cancer, sarcoma, and certain innocent tumours by internal administration of arsenic might be held as proof of the neurotic hypothesis, but there is another explanation of its action upon the malignant tumours. Whether or not this explanation applies to innocent tumours it is impossible to decide. This matter cannot be discussed until we reach a later chapter, but it may now be hinted that the second explanation of its action is that it alters the reaction of the blood. Potassium iodide, another nerve medicine, has sometimes a retrogressive effect upon cancer. Epithelioma has been cured by the actinic rays and adenoma sebaceum benefited. The X-rays have cured some cases of warts and have ameliorated lipomata.

An objection which will be made against the neurotic hypothesis is that so many cancer patients appear to be in perfect health. I have already pointed out the possibility that powerful agents may upset even the most perfectly-balanced nervous system, and yet another answer may be put forward. If unilateral hyperidrosis occurs among the apparently healthy, and other abnormal nervous states, why not the nervous instability which predisposes to the development of cancer ? And the same question may be asked for innocent growths.

Another objection that may be urged is that a long interval of time sometimes elapses between the onset of malignancy and the action of a trauma. The following suggestion is a somewhat feasible one. The trauma weakens the local nerve-supply, but not sufficiently to paralyse its control over the tissues. In the course of time, with advancing senility or exposure to conditions which have generalised neurotic effects, the nervous system breaks down at its most unstable part.

It is undoubted that worry and anxiety—nerve-depressing influences—predispose to cancer. And it is important that a crop of warts may disappear in a night after severe emotion. But I am afraid that the predisposing effect of civilisation, with its train of neuroses, is not yet proven. I can urge a number of reasons why cancer should be rare among uncivilised peoples, and I can cite evidence to the same effect, yet it is a matter of fact which can only be decided after adequate inquiry, allowance being made for differences in the expectation of life, in the freedom of access to medical advice and the desire to make use of it, and in the exposure to traumata, among those peoples as compared with the civilised. A point which I have had under consideration is that neoplastic tendencies among uncivilised peoples affect mesoblastic elements more than the epithelial. This was suggested by the statement that in the United States of America fibrous growths are commoner among the negroes. There is the same tendency among idiots.

In addition to the direct effect of the above depressing influences, there is the indirect effect of encouraging chronicity of inflammatory states.

CHAPTER XXI.

EARLIER REFERENCES TO THE NEUROTIC HYPOTHESIS.

UPON taking up a typical work on pathology which professes to discuss the etiology of tumours and the various hypotheses advanced respecting their nature, it will in nearly all cases be found that the parasitic, embryonic-rest, and tissue-tension hypotheses are mentioned, but that the neurotic hypothesis is ignored. In Wolff's monumental history of the cancer question only a casual reference is made to it. When, after working for some time upon a mistaken hypothesis, I discovered the existence of arsenical cancer—also, it may be said, generally ignored—and its significance, and I had correlated most of the known facts with the neurotic hypothesis, it eventually became necessary for various reasons that a more thorough examination of the cancer literature should be made. During my search it greatly surprised me to find that so many had already suggested a neurotic basis for cancerous and other neoplasms, and it was a sore disappointment that I had been preceded in working out some of the applications of the hypothesis, so that my time had been wasted to some extent.

The first undoubted suggestion of a neurotic hypothesis which I can find was made in 1889 by Parsons: "Let an injury or irritation to some part of the body occur . . . an active formation of cells takes place, until the injury is repaired or the irritation removed. Now this formation of new tissue is essentially a new growth, although not a tumour. The capacity for forming it is common to all the tissues of the body, and it ceases when the necessity for its continuance has disappeared. This appears to show some controlling influence, probably by the nervous system. Is it not, then, possible that all tumours are in the first instance composed of cells formed in the normal process of repair, but that, having escaped from the control of the nervous system, they take an independent life, and continue to proliferate and develop without check, just as all living cells are capable of doing *ad infinitum* under favourable conditions? The frequent association of cancer with a depressed condition of the nervous sytem is explained by this hypothesis."

Following Parsons in the same year, Marshall also advanced an hypothesis which was not neurotic in the true sense, for he did not suggest abnormality on the part of the nerves, but an excessive proliferation of the tumour cells with which the nerves could not maintain touch: "Now, what is the great governor of the body?

The nervous system. . . . I believe strongly and firmly that the nervous system is the centre which lays down and commands the growth of the body in this, that, or the other direction. . . . Has anyone ever shown, as distinctly as has been shown with regard to the secreting cells, that the epidermoid or epitheloid cells of cancer are under the influence of the nervous system? . . . I cannot believe that when they are aggregated into these irregular masses and groups, when they penetrate along the lymphatic spaces as they do through the body, when they reach the lymphatic glands far away from any primitive nerve-fibre which could possibly have once reached them, when they advance into distant tissues, when they recur in a cicatrix—I cannot admit without actual demonstration that the nerve-fibres go on with them, so as to regulate their disordered and anarchic government. . . . We want to know this, and here is work for the microscopist. . . . I suspect what the answer will be, from my own crude investigations. I can hardly suppose that, in the pell-mell agglomeration which we see in a cancer, each cell has its own proper guiding nerve-fibre. How and why may we suppose that these nerve-fibres are severed? It may be simply from the extreme rapidity of the cell growth; and this may afford one indication of the mode in which cancer originates from a comparatively healthy tissue. In the healthy formation of epithelial tissue the nerve-tissue would still remain in it, but in the overgrowth excited by some long-continued injury at last the cells break away from the nerves."

In his work on "Cancers and the Cancer Process," Snow elaborated an "autositic" theory in the following terms: "Inasmuch as the nervous system was not only the controlling agency by which transformation of embryonic cell units into more or less specialised tissue originally took place; by means also whereof the healthy balance of component elements is maintained through the somatic life of the organism; it further seems permissible to regard this 'cancer process' as essentially consisting in a local 'cell rebellion,' certain cells casting off their allegiance to the central authority." The first part of the sentence is, of course, pure assumption, and is an open question; the second part, if it is a re-statement of the trophic theory of nerve action, is also an open question, though the neurotic hypothesis of the origin of cancer is dependent upon it; the third part ignores the state of the nerves which allows the rebellion to take place. But further on in the work the latter deficiency is supplied, for it is stated that the "autositic" theory "derives confirmation from the influence of neurotic conditions in generating some prevalent forms of cancer; from the liability of organs conspicuously influenced by emotion (as the uterus and mammæ) to malignancy, and the preponderance of the more emotional sex among cancer sufferers; from the tendency of special organs, which have passed their functional prime and are undergoing involution, to the cancer process; from the rapidly-increasing prevalence of cancerous diseases among civilised communities; perhaps even from the relative immunity of savage races, of lunatics and idiots."

Green, in "An Introduction to Pathology and Morbid Anatomy," describes the neurotic hypothesis as being somewhat visionary, for so little is known of the action of the nervous system on tissues. In favour of the hypothesis are noted: the supposed greater frequency of tumour formation in man and the higher animals than in those lower in the scale—the development of tumours being thus *pari passu* with that of the nervous system; the absence of nerves from tumours; the facts that tumours have no function and that they grow independently of the other parts of the body, often flourishing luxuriantly while the rest of the organism is much emaciated—the latter peculiarity appearing to depend on some freedom from central control. Also referred to is the connection of molluscum fibrosum with nerve distribution, and the work of Campana and Cheatle.

Noting the occurrence of cancer in neurotic families and the common origin of the nerves and epidermis from epiblast, and noting also the earlier work of Cheatle, various other considerations are advanced by Shaw which he looked upon as backing up the view that neurotic heredity is the chief predisposing cause of cancer: the fact observed by D'Arcy Power that, after operation, recurrence is diminished in frequency and postponed by change of scene and surroundings, which is well known to be a successful measure in treatment of diseases of the nervous system; the beneficial action of radium on some malignant and certain nervous diseases; the simultaneous increase of cancer and functional nervous diseases in civilised communities, and the markedly greater incidence of cancer in certain urban (Australian metropolitan) than in the surrounding districts (syphilis, alcoholism, and tuberculosis being much more probably co-results with cancer of urban life than causes of the disease); and the rarity of cancer as well as of nervous diseases among savages.

Wilson, speculating upon the nature of cancer, proceeds: "May we think that the presence of nerves in metazoa acts like a brake or check on cell proliferation? . . . Owing to lessened function, the nerve cell has probably neither the time nor the ability to keep pace with the epithelial cell, which from irritation proliferates rapidly and finally frees itself from nerve influence."

Galloway drew attention to the pigmentation in certain precancerous states, and suggested that, if it were conceded that the distribution of pigment is under the influence of the nervous system, the abnormal process might continue and the disorganisation of nervous control end in allowing the resistance of the connective tissue to be impaired and the epithelium to escape from control.

In the course of a speculative paper, Wade remarked as follows: "I submit that there is good reason to suspect that the origin of cancer may be intimately connected with senile changes in the nerve-endings, or in the cells, or perhaps with both combined."

At some period, of which I have not yet found the date, Rivière pointed out that the origin of cancer is comprised in a direct insufficiency of the nervous system at a determinate part of the economy. Broussais, Amussat, Barras, and Kolk also held to the neurotic hypothesis.

I anticipate that in the Continental and American literature there will be many references to a neurotic hypothesis, but to unearth them is more than what I am at present prepared to undertake. In the preceding chapters there have already been repeated some of the suggestions of a neurotic hypothesis as applied to certain forms of innocent tumours.

CHAPTER XXII.

SOME PHYSIOLOGICAL ASPECTS OF MALIGNANCY. REACTION OF POTENT SUBSTANCES.

AT an early stage in my pursuit of this present line of research it was evident to me that the potent chemical media directly inducing malignancy must be somewhat alkaline or basic, though it is apparent that these media cannot be so powerful as to be caustic in action. Some of the following facts were my justification in coming to this conclusion.

Moore and Wilson find that in cases of malignant disease—carcinoma, epithelioma, rodent ulcer, and sarcoma—the alkalinity of the blood-serum due to inorganic constituents is higher than normal, and they suggest, on the ground that the difference in direction of increased alkalinity is less after removal of the protein than before its removal, that the proteins possess a higher basic reactivity. They also draw attention to the fact that there is an increase in alkalinity of the serum in old age, when the organism is more liable to the onset of malignancy.

Now, certain febrile diseases are antagonistic to and retard malignancy, and these diseases are marked by a diminished alkalinity of the serum. Pyrexia of unknown origin has appeared in cases of cancer, and has proved antagonistic. As already pointed out, cancer and tuberculosis are frequently associated together in the same family, yet they have an antipathy for one another which is manifested by their somewhat rare occurrence together at the same time in the same person. The explanation may be that the febrile condition in cases of tuberculosis spells for a change in the reaction of the serum. Tests of the serum in tuberculosis miliaris accompanied by high fever are too few in number to enable us to dogmatise, but they indicate a lowered alkalinity.

Gout, in which the alkalinity of the blood-serum is lessened, appears to be antagonistic to cancer.

Diabetes is apparently another disease which is somewhat incompatible with cancer, and the information available encourages the supposition that a consequent change in the reaction of the blood affects the growth.

The antagonism of malaria to cancer may depend upon a change in the reaction of the blood-serum.

The presence of suppurating wounds in the body, and inflammation near to the growth, induced by irritants or the cautery, may result in retardation of the growth and may lead to cure. In the eighteenth century surgeons made an issue after operating for malignant disease. They also, it may be said, inoculated with syphilis, but I cannot find evidence to prove there is a lowering of alkalinity in any stage of this disease, though it is not improbable. When suppurating conditions are present, a febrile state may arise, and there is a lessening of free carbon dioxide in the blood, so that we may expect a change in the reaction of the serum. Erysipelas, with which is associated a febrile state and a more acid urine, is antagonistic to malignancy. Coley, of course, uses cultures of two parasites—one the essential agent in erysipelas, the other constantly present in suppurative conditions. His treatment ameliorates sarcoma as well as cancer.

Amelioration of cancer during lactation has been reported. It is certain that the formation of an alkaline secretion will lessen the alkalinity of the blood-serum.

It has sometimes been remarked that many cancer patients are at the onset of the disease florid and well-nourished in appearance, and that, speaking relatively, anæmic individuals escape attack. Lomer believed that the cancerous cachexia and anæmia have an influence in checking cancer. Of course, in pernicious and some other forms of anæmia the alkalinity of the serum is diminished.

An old method of treatment for cancer is by starvation, but so far I have been unable to discover the complete history of this method and why it was deserted. Our interest in it lies in the fact that starvation leads to a condition of acidosis. During the potato famine in Ireland the death-rate from cancer was lowered. The semi-starvation once, if not now, practised in workhouses and prisons, leaving its mark in the anæmic condition of the inmates, may account for the relatively low death-rate from cancer in these institutions. But in the case of the prisons I would like to be assured that the vital statistics are not affected by the practice of liberating prisoners about to die.

Clowes and Frisbie report that rapidly-growing adenosarcomata of mice have a high content of potassium and a small content of calcium, while the conditions are reversed in the slowly-growing tumours. It is asserted by more than one observer that the proteins of malignant growths are less easily coagulable by heat than those in normal tissue cells, and the suggestion is made that they are of the nature of albumoses. But this greater resistance to the coagulative effect of heat is also characteristic of alkali-albumens, so that it is possible that the proteins of malignant cells have a more basic reactivity than the proteins of normal cells. If this is the case, it is manifest that the condition of the blood will be especially conducive to successful growth on the part of the neoplasm. If it is not the case, it can still be urged that the metabolism of the neoplasm will be encouraged, for a somewhat higher alkalinity of the medium bathing cells tends to render their metabolism more active.

It is thus clear what is the reaction of the blood-serum in cancer—we should almost use the broader term malignancy—and whether or not the metabolism of the cancer cell has a more basic trend than the normal, we can understand that, acting along with the change in the blood reaction, antecedent hyperalkalinity in the place of origin of a cancerous growth will encourage its development. The seats of chronic inflammation, more particularly the catarrhal, are exposed to higher alkalinity than the rest of the body, though I take it that this is a general statement which does not always apply. The seats of ulceration are generally more alkaline, and pus is generally alkaline, though it may be acid or neutral owing to the presence of certain bacteria. When, therefore, malignancy supervenes in the seats of inflammation and ulceration, it is probably due in part to local hyperalkalinity. Of course, it is by withdrawal of bases from the blood that its reaction changes under these conditions, and it will be urged that if the reaction is thus changed malignancy ought not to supervene. But it does supervene, and the matter probably hinges upon the degree with which local hyperalkalinity is increased as compared with the degree with which the reaction of the blood-serum is altered. When bases are withdrawn under these circumstances, the effect will be less upon a bulky medium, such as the blood, than within a circumscribed area of inflammation. Further, the onset of hyperalkalinity of the blood-serum with old age, or from other causes, may be too pronounced to be checked sufficiently in this way.

Our next duty is to consider the part played by the organic decomposition products and alcoholic liquors in affecting the reaction of the blood-serum or the local tissue reaction. What we have to learn is the general reaction in each case of the mixtures of compounds—tar, oil, pitch, beer, &c.—which are potent, and, where the finger can be pointed at isolated compounds, whether these are acid or alkaline.

Now, coal contains more nitrogen than wood, and the larger percentage of nitrogenous bases presumably present in coal-tar will account for its alkaline reaction, that of wood and peat-tar being acid. Shale-tar also is alkaline in its reaction. The pyridine bases are in less quantity in wood-tar oils than in coal-tar oils. In the case of "tarry water," that got from wood-tar is acid in reaction, that from coal-tar is alkaline. Coal-tar pitch and shale-tar pitch are both strongly "alkaloidal," and melted coal-tar pitch evolves ammoniacal fumes. That the combined decomposition products of coal tend towards alkalinity, while those of wood are more acid, might be taken as a sufficient explanation of the fact that scrotal epithelioma among chimney sweeps is almost unknown in countries where wood is used as a fuel and is commoner where coal is used. But the difficulty is that aqueous extracts of samples of soot obtained from Manchester and London respectively by Professor Knecht were both strongly acid, and, further, an aqueous extract of lignite soot obtained from Prague was neutral to litmus. Now, the soot from stone coal is more potent than that from lignite. Can we then urge that malignancy is more likely to begin in parts which are bathed in alkaline media than in parts which are bathed by acid media? Of course, I am referring here to the decomposition products alone, the blood-serum being left out of account. But the statement anent the reaction of these aqueous extracts may be tempered in two ways: the lime in the soot was not dissolved out, yet it may affect the reaction of the soot; and, further, the samples of soot taken may not have been typical for each kind of coal. It might seem that the appearance sometimes of eczema, and warts in other cases, upon the scrotum and other parts of the body in sweeps is an indication that soot varies in quality. Those shale-workers engaged in refining the paraffin-wax with naphtha are especially liable to cancer, and the paraffin-wax and naphtha probably resemble the tar in their reaction. Very important is the inception of malignancy in the bladder in workers inhaling the vapour of aniline as well as that of toluidine, nitrobenzene, and nitrotoluene. There will be increase of the alkalinity of the blood-serum and urine during the working hours.

While we should expect the potency of heat decomposition products in the causation of malignant tumours to be correlated with alkalinity (basicity), definite proof is not to be obtained. Obscuring this question of reaction is that of the relative effect upon the nerves; for, it being probable that coal-soot contains a larger percentage of nitrogenous bases than wood-soot, the former may have more decided and characteristic effects upon the nerves than the latter.

The emanations from manure, sewage, and putrefying flesh are generally, if not always, alkaline, and this is probably also true, owing to the increased formation of ammonia and fatty amines, of those from wet and clay soils. It has been proved in the case of rabbits that the inhalation of ammonia and trimethylamine leads to a temporary increase in the alkalinity of the blood-serum. Human and herbivorous fæcal matter, fresh and old, has an alkaline reaction, so also has stagnant human and fresh and stagnant herbivorous urine. Sometimes gastro-intestinal fermentation renders human urine more acid, and if this is really the case, the reaction of the blood should be altered in the same direction.

Beer is slightly acid, and trade methods are adopted to prevent too great an acidity. The change of the fatty acid content to carbonates in the blood ought to increase the alkalinity of the serum, yet there is a complication in the formation of uric acid. The statement is made that acute alcoholic intoxication renders the blood less alkaline owing to the formation of volatile fatty acids, but this can only be temporary. Whisky is very slightly acid, and its fatty acids will combine with bases so that carbonates will form in the blood, raising its alkalinity. Now, as regards the state of affairs in the stomach : both forms of liquor are acid in reaction; their contained alcohol and carbohydrates will ferment, acids being formed; and gastritis, following their excessive imbibition, may be accompanied by hyperchlorhydria. Acting together, these are strong factors as against the local tissue alkalinity incidental to catarrh and the hyperalkalinity of the blood-serum, and they may be obstacles to malignancy in the stomach.

Rather than leave this part of the subject untouched, these notes upon the reaction of the decomposition products have been included, though I would have been happier had it been possible to make them more conclusive. More extensive data are necessary.

That mechanical and physical traumata cause cancer, and do so without altering the local tissue reaction except by inducing inflammation, does not invalidate the above discussion.

There should not be any difficulty in believing that malignancy appearing within seats of inflammation is merely a continuation of a process of abnormal proliferation which sometimes goes on under such conditions. In catarrhal conditions there may be active proliferation of the epithelial cells, as well as of the derived glands, when there is exudation from the vessels below, with pus cells escaping. Hypertrophy and atrophy may be found together in the same lesion, and in eczema, psoriasis, and lupus, along with cell destruction in the Malphigian layer may occur hypertrophy of the interpapillary bodies below.

CHAPTER XXIII.

THE TREATMENT OF MALIGNANT DISEASE.

WHILE excision, or treatment with caustics, the cautery, the X-rays, or radium emanations may sometimes prove successful methods of dealing with malignant disease, they fail in the majority of cases owing to the impossibility of reaching the secondary growths and outlying parts of the primary growth, so that it is to a constitutional method of treatment that we must look for ultimate success. Our hopes are engendered by the knowledge that malignant growths in some cases retrograde spontaneously, and facts already given point towards the conclusion that their metabolism is upset by a change in the chemical condition of the blood-serum. How to make this change it is now my purpose to suggest.

Moore and his colleagues summarily dismissed the method of administration of mineral acids on the ground that the reaction of the blood is determined through the agency of the liver and kidney cells, and if these have been set at a definite wrong level of action, the regulating mechanism of the body is then at work against change of the action by therapeutic means. Only with large and continued doses of acid, and on approaching the limits of acid intoxication, can any diminution of the alkalinity be hoped for, and as soon as the acid administration is slackened, the acid is neutralised by ammonia obtained from oxidised protein. And the difficulty is to maintain H ion concentration in the blood plasma permanently at a high level against the competition of the kidney and other cells of the body which are tending to reduce it to its old vicious level.

To me the assumption that a permanent change is necessary appears to be unjustifiable, for there is no evidence whatever to show that more than a temporary change is called for—a change lasting only during the duration of the disease. As the method of lessening the alkalinity of the blood by acid administration does not seem to have been tried, would it not be better to give it a trial, in spite of discouraging assertions of its futility except with excessive and distressing doses? A survey of the literature affords proof that hæmalkalimetry is liable to pronounced sources of error, and we should not allow any consideration to stand in the way of a practical test in such a serious matter.

I have some doubt as to the amount that should be given. Owing to the protective formation of ammonia—and when phosphoric acid is administered, the tendency for some of the disodium phosphate in the serum to be replaced by monosodium phosphate, which diffuses rapidly into the urine, so that relatively little alteration is made in the reaction compared with the amount of acid given—it therefore may be necessary that somewhat large doses should be administered. Dunlop has shown that such doses increase the total amount of bases in the urine, the effects lasting for hours only or for days afterwards. On the other hand, acids are prescribed in more modified doses in order to prevent the formation of phosphatic calculi, and to modify irritation from hyperalkaline urine—in the latter case acting also as antiseptics, and thereby inhibiting alkaline fermentation of the urine—on the ground that the reaction of the blood is altered, and necessarily that of the urine, which is directly dependent upon it. Thus some alteration results from smaller doses, though they are freely given, and the change may be quite sufficient, for a very slight change in the reaction of the serum resisting detection may have decided effects upon cell metabolism. And it is to the more modified doses that we ought first to give a trial, turning to the more drastic method if they fail. As a malignant growth usually takes a long time to increase in size, we ought to be content to make it retrograde as slowly.

There are some disadvantages pertaining to the administration of acids by the mouth. Being irritants to the gastric and intestinal mucous membranes—through which, by the way, they rapidly diffuse—after prolonged use catarrh may be induced, while the secretion of gastric juice may be lessened. Another disadvantage is their tendency to combine with bases in the food, and to form acid-proteid combinations. But by rectal administration, after flushing out the fæcal matter, the strain upon the stomach can be lightened and the difficulty of neutralisation partly surmounted. Another method of administration is by intravenous injection. And in the case of accessible growths, by injection into them, or by direct application of the acid, the latter will exercise a caustic influence, and may also in a very slight degree become absorbed into the circulation. Some or other of these alternative methods can be used simultaneously in order to distribute the strain. The tendency of mineral acids to slow the pulsations of the heart and paralyse the respiratory centre, and the endocarditis sometimes following their injection, will have to be remembered. Nitric, phosphoric, and benzoic acids may induce skin rashes.

We may now consider what acid or acids will be most useful. There is no fact, as far as I am aware, indicating a specific acid as one most likely to derange the metabolism of the cancer cell, and it will probably be found that the administration of different acids simultaneously by different methods will be best, for excess of a single acid will have a greater disturbing effect upon the system.

Somewhat naturally we first turn to the mineral acids, of which at least the four cited lessen the alkalinity of the blood and increase the acidity of the urine, or lessen its alkalinity in cystitis, when administered freely by the mouth. They also prevent the formation of phosphatic calculi. Hydrochloric acid is marked off from all other acids by its greater efficiency as a gastric adjuvant, and it will be particularly useful in a disease which is characterised by its absence from the gastric secretions. Sulphuric acid does not appear to have anything to recommend its preference before other mineral acids, and the same is true of nitric acid. Orthophosphoric acid, though less liable than the other mineral acids to induce gastro-intestinal catarrh, which allows its administration in larger doses, is a more feeble acid. Joulie has taken 27 grammes of the officinal acid without being distressed. Acid sodium phosphate alters the reaction of the urine, and may be useful.

Among the organic acids we may reject the nitrogenous, which will increase the amount of amidogen, while they are feeble acids. The non-nitrogenous fatty acids are out of court, for, after combining with bases, they are oxidised to carbonates, which increase the alkalinity of the blood.

The non-nitrogenous aromatic acids promise more, for at least some of them increase the acidity or lower the alkalinity of urine, though partly because of their antiseptic action. They are excreted in the urine as derivatives of uric acid, in many cases, after combining with glycin, as hippuric acid, which is abundant in the urine of persons suffering from febrile diseases. Of course they are feeble acids.

It is to cinnamic acid that I first turn, for the following reasons. Drage reports improvement following upon the use of oil of cinnamon, and believing that the leucocytosis produced was responsible, he is experimenting with the sodium salts of cinnamic and coumaric (orthohydroxycinnamic) acids, and tylmarin, an acetyl derivative of orthocoumaric acid. But as uric acid excretion is increased in leucocytosis, which occurs also in febrile and suppurative conditions, he may unconsciously be altering the reaction of the blood. He was certainly doing this in another way when using oil of cinnamon. The oil varies in composition within narrow limits according to the part of the tree from which it is extracted and the locality from which it is obtained, while the passage of time after its extraction allows some small portion of the principal constituent to become oxidised. This constituent, by far the largest, is cinnamic aldehyde, which is oxidised to cinnamic acid. When administered, the aldehyde is partly oxidised in the blood to benzoic acid—I am not clear whether or not it is first changed to cinnamic acid—which, after combining with glycin, is excreted in the urine as hippuric acid. The remaining constituents of the oil are mostly terpenes. It is not noted by Drage that cinnamon oil had previously been used to relieve pain in cases of cancer, with varied results, the patients asking that its use be stopped. The highly-flavoured constituents of the oil render it somewhat nauseous when taken continuously, but cinnamic acid alone is described as being tasteless, inodorous, and innocuous. It is sparingly soluble in water, more readily in alcohol, glycerine, and olive oil. Coumaric acid is easily soluble in water, but is inaccessible for therapeutic purposes. For antiseptic purposes a five per cent. aqueous solution of cinnamic acid and a solution of one part of the acid to ten or twenty parts of glycerine have been used as injections in tuberculosis, and that the acid is used as an antiseptic renders necessary a qualification of the statement that it is innocuous.

Benzoic acid, of which cinnamic acid is a derivative, appears to be less innocnous than the latter. Yet, though doses of six to eight grammes (92 to 123 grains) have caused nausea and vomiting, larger doses have been taken without the manifestation of these effects. In two days Schreiber took fifteen grammes (230 grains), experiencing various mild symptoms of distress. Wiley's recent results indicate a much lessened degree of toleration. I suppose that the latter will depend upon whether the synthetical or the natural acid is used.

A number of somewhat inaccessible aromatic acids have been experimented upon with different objects in view, but, after all, I am in doubt about the efficiency of the aromatic as compared with the mineral acids.

There are three substances—arsenious acid, phosphorus, and potassium chlorate—which have received the credit of curing cases of malignant disease when administered internally, with the addition, in the case of arsenious acid and potassium chlorate, of application to the growth. These three substances in poisonous doses induce acidosis, and it is probable that they will have some effect in therapeutical doses. A weak acid such as arsenious acid can have little effect, acting as an acid, upon the reaction of the serum. Winiwater asserted that when arsenic was injected, the local effect of injection and the arsenical fever contributed to the diminution in size of the tumour. In the case of accessible growths, a phosphorated oil should form a useful caustic, for some of the phosphorus may enter the blood. These substances may produce their effect partly by action upon the nervous system. The fact that arsenic induces cancer does not preclude its trial. It will be urged that, by altering the reaction of the blood, it should not allow cancer to develop. This effect can only be temporary, and it may not affect pronounced hyperalkalinity in a sufficient degree ; yet this will not prevent its use to reinforce other methods.

I have found a statement to the effect that some compounds of sulphur, themselves neutral in reaction, when given by the mouth, raise the acidity of the urine, a rise which lasts for some little time.

The suggestion is made that the sulphur is oxidised with the formation of an acid, presumably in the blood. Hyposulphite of sodium is one of these compounds.

The above methods may be reinforced by others which are more natural. Most important are the dietary methods of lowering the alkalinity of the blood-serum. Vegetables, especially green vegetables, should be excluded, on the ground that they reduce the acidity of the urine or even render it alkaline, for we know that the reaction of the blood must also be altered. They contain a relatively large proportion of bases in combination with fatty acids which become oxidised in the blood to carbonates. Fruits can be objected to for similar reasons, in spite of their acidity. It has been asserted that a purely carbohydrate diet increases the alkalinity of the blood. An excessive meat diet increases the acidity of the blood by giving rise, it is said, to incompletely-oxidised acids, such as uric acid, which cannot be excreted as such, and which combine with alkali in the serum. As the thyroid gland is rich in nucleo-proteins, does it modify cancer by forming an excess of uric acid ? A similar question may be asked of lymph-gland extract and protonuclein. The latter is administered for the purpose of inducing leucocytosis. The sulphur and phosphorus of the proteins are also oxidised in the body to sulphates and phosphates respectively, and the consequent removal of alkali also tends to reduce the alkalinity of the blood-serum. But there is another reason why an excessive meat diet is preferable to an excessive vegetable diet : there is a relatively small proportion of bases contained in meat as compared with the amount contained in vegetables. An excessive meat diet is thus indicated, but the meat should be boiled in more than one change of water in order to extract the nitrogenous bases which begin to form after death as a result of bacterial action. While the ash in the food should be kept low, it is well to remember that there is danger in a diet too free of ash, owing to the severe acidosis resulting.

The method of treatment by starvation probably depended partly upon the failure of the supply of bases to replace those removed in the excretions. Starvation is out of the question, owing to the consequent debility, but the supply of food can be kept as low as possible. The modification of cancer during fevers may be due in a degree to partial starvation.

Reyburn asserted that the frequency of cancer was lessened by hard manual labour. Now muscular exercise reduces the alkalinity of the blood, especially when the diet contains little or no protein. There is little or no alteration when the diet is rich in protein. As a purely carbohydrate diet is said to increase the alkalinity of the blood, we are on the horns of a dilemma, unless a happy mean can be found. Yet our facts may be wrong, for many mistakes have been made in hæmalkalimetry. The most sensible course would be to give the patient abundant exercise, if his condition allows it, whatever the diet may be.

The acidity of the urine is lowered when the oxygen in the air is below the normal, and thus not only may precautions be taken to ensure fresh air for the patient, but inhalation of oxygenated air would be an advantage.

Some advantage would also be gained by the use of distilled water instead of ordinary tap water.

I have thus indicated a number of methods by which the alkalinity of the blood may be diminished. They are not all of equal value, but idiosyncrasy will in practice reduce their number so that some dependence may have to be placed upon the least valuable. It may be urged that a dietetic method will impose the least strain upon the patient, and that a protein diet poor in bases will the most efficiently lead towards a condition of acidosis, but there is the question of toleration. For example, egg yolk is exceedingly poor in bases, yet it is not readily tolerated, and this applies, in a less degree, to an excessive meat diet. A lean meat diet was administered for periods of some months by Salisbury in cases of cancer, with apparent improvement, it is said, in general health ; as far as the cancerous growths were concerned, favourable reports were given, but this method of treatment was allowed to lapse. A concerted attack upon the reaction of the blood, this method being applied along with others, may result in a sufficient degree of alteration. It may be that the failure of a single method depends upon its effects lasting only for a brief period. The successive application of a number of methods would obviate this difficulty.

Guidance as to place of residence may be obtained from a perusal of Chapter IV.

CHAPTER XXIV.

SOME OCCUPATIONAL GROUPS NOT PREVIOUSLY CONSIDERED.

UP to the present there has been omitted any reference to other occupational groups than those considered in the earliest part of this work, and this for more than one reason. In the case of some occupational groups the nature of the potent agent or agents is not readily apparent and is a matter of discussion; and where a number of agents are concerned, it was impossible earlier to deal with these groups, as some of these agents were only considered in later chapters. While it would be desirable that a fairly complete survey of these groups should now be made, to demand this of me is more than what is reasonable, looking to the numerous factors involved in many cases, and the difficulty of treating them exhaustively. Further, the groups occupying the lower part of the tables owe their position partly to absence of the essential occupational traumata, partly to an excessive death-rate from other causes. It seems to me sufficient, therefore, that only those occupational groups with a high average position in the table during both periods should be considered.

General Labourer [*Cancer*—55 (51), 111 (63); *Alcoholism*—16 (15), 40 (16)].

The general labourer resides under relatively insanitary conditions, usually in old houses situated in narrow streets and close courts, and not infrequently in the neighbourhood of stables and works which are under our suspicion. The employment will sometimes be of an insanitary nature or otherwise objectionable, but it is more than probable that this is counteracted by the open-air conditions under which many of the general labourers work. In this group are many individuals of a somewhat degenerate type. The death-rate from alcoholism is high, and these workers freely use the short clay pipe. The great difference in the cancer incidence between the two periods is difficult of explanation when such a numerically large group is under consideration.

Merchant Seaman [*Cancer*—69 (51), 103 (63); *Alcoholism*—25 (15), 26 (16)].

Unna's "sailor's skin" has already been mentioned. The sanitary arrangements of the forecastle are poor and ventilation is imperfect, while at one time overcrowding was the rule. The air in ships' holds is bad, partly because of the emanations from the bilge water which pervade the whole of the ship, sometimes from the nature of the cargo, which may even be one of manure. Live stock occasionally is carried. Some docks and tidal rivers are practically equal to open-air sewage tanks. Obstinate constipation is one of the results of a seafaring life, and sailors are also liable to mechanical traumata and venereal disease. The frequent changes from forecastle to inclement conditions outside, and the reverse change, must aggravate inflammatory processes and encourage neurotic conditions, especially of the skin.

Tinplate Manufacturer, Tinplate Goods Maker [*Cancer*—60 (51), 95 (63); *Alcoholism*—11 (15), 10 (16)].

Before being dipped into the molten tin, the plates are cleaned in dilute sulphuric acid. The acid fumes irritate the throat and eyes and induce nausea and vertigo. The workers are exposed to great heat from the molten tin, which must evolve some arsenical vapour. More female than male labour is employed for the cleaning with sulphuric acid. I am without information of details of the making of tinplate goods.

Chemical Manufacturer [*Cancer*—63 (51), 85 (63); *Alcoholism*—8 (15), 4 (16)].

The men employed in some branches of the manufacture are exposed to the attack of irritating fumes, liquids, and dust, so that they suffer from skin sores and troubles of the respiratory passages and gastro-intestinal tract, and it must be through this irritation that they are more liable to cancer, for the statistics prove that they suffer less than " all occupied males " from nerve troubles.

Law Clerk [*Cancer*—71 (51), 72 (63); *Alcoholism*—25 (15), 8 (16)]
Barrister, Solicitor [*Cancer*—69 (51), 69 (63); *Alcoholism*—15 (15), 13 (16)].

A large number of those engaged in the pursuit of the law are to be found in cancerous London. Out of 19,978 barristers and solicitors in England and Wales in the year 1891, there were 5,454 in the registration county of London, while there were 9,005 out of 27,374 law clerks. In the same year there were 1,515,544 males of the age of ten and upwards in the registration county of London and 10,591,967 in England and Wales. Lawyers are subject to the action of " crowd poison " in courts, and it has been said of the air of a typical London police-court that it is strikingly impure and has a disagreeable odour owing to emanations from the bodies and clothing of a certain class. I have considered the possibility of the unremitting attendance sometimes required in the courts leading to enforced retention of fæcal matter, the effects being added to by the constipation incidental to a sedentary life; but this is a matter upon which I cannot make a decision. It is an old idea that excessive mental labour predisposes to cancer. It is probable, but where is the proof?

Bookbinder [*Cancer*—69 (51), 71 (63); *Alcoholism*—18 (15), 16 (16)].

In the year 1891, out of 11,487 male bookbinders in England and Wales, there were 6,409 in the registration county of London. The bookbinder works in rooms generally ill-ventilated and pervaded with the fumes from gas-stoves and the emanations from heated glue and size. The death-rate from nervous diseases is below that for "all occupied males," and I may take this opportunity of suggesting that there may be, as it were, competition among different diseases to carry off the most victims, so that in the case of some occupational groups some one or other of the general neurotic diseases come off second best, and maybe, as in the case of bookbinders, one of the neurotic diseases—cancer—escapes.

Commercial Traveller [*Cancer*—72 (51), 67 (63); *Alcoholism*—26 (15), 21 (16)].

The commercial traveller respires the air of licensed premises to a considerable extent. For more than one reason railway journeys induce constipation, and in going his rounds the traveller is at a disadvantage in obeying the calls of nature.

Textile Dyer, Bleacher, &c. [*Cancer*—60 (51), 79 (63); *Alcoholism*—12 (15), 11 (16)].

Manure, urine, and sodium arsenite, among other substances, are used in dyeing processes as mordants. Arsenic and aniline have been identified as impurities in dyes, but as toluidine, xylidine, diphenylamine, naphthylamine, acridine, and other organic compounds are used in dye-making, they also will be present as impurities. Dyers suffer from eczematous and other skin eruptions, and it is the arsenic which receives the blame. It is true that arsenic does not now enter into the process of aniline dye-making, but we are dealing with periods when it did. The dyer is liable to catarrhal troubles from exposure to high temperatures. The bleachers suffer from the irritative effects of the bleaching agents, manifested upon the hands and arms and in the bronchial tubes.

Currier ; Leather Goods—Maker, Dealer [*Cancer*—70 (51), 68 (63) ; *Alcoholism*—11 (15), 9 (16)]. *Tanner, Fellmonger* [*Cancer*—43 (51) ; *Alcoholism*—9 (15). 1890–2 *only*]. *Tanner* [*Cancer*—33 (63) ; *Alcoholism*—11 (16). 1900–2 *only*]. *Furrier, Skinner* [*Cancer*—111 (63) ; *Alcoholism*—23 (16). 1900–2 *only*].

The currier receives the undressed leather from the tanner, and, except in the case of leather intended for soles, works into it various oily and greasy substances. His duty it also is to apply the composition which gives the glazed surface to patent leather. For these purposes are used mineral oils, aniline oil, birch-tar oil, bone oil, asphalt, vegetable oils (turpentine, linseed, castor, olive), animal oils (sperm, cod-liver, neatsfoot), hot fats (beef tallow, wool grease), glue, blood, ammonia, &c. Chamois leather is prepared by the currier by steeping in fish oils, some degree of decomposition being allowed, and the putrefied oil (degras) afterwards expressed from it is also used in currying. The currier is subject to skin eruptions, and currying is reckoned a public nuisance—an obnoxious business.

As concerns the other occupational groups included in the heading, an alteration in classification is to be noted. The classification of the occupations adopted for the first period was that of the census of 1891, for the second period that of the 1901 census. In the latter the fellmonger ceased to exist as such, and was classed with the "tanner," "furrier, skinner," "currier," or "dealer in skins, leather, &c.," according to the use of the respective terms in various districts. Yet we may take it that the "tanner" of the second period is practically equivalent to the "tanner, fellmonger" of the first. The "furrier, skinner" was not included in the table for the first period, and the "dealer in skins, leather, &c.," was not considered in either supplementary report.

The duty of the fellmonger working in a tannery is to prepare the skins for the tanning process. From fresh skins fat and fleshy matters have to be removed, and dried skins need to be soaked in water. In the next stage the skins are left to steep in pits or tanks along with lime, which may be gas-lime, sometimes also with added orpiment or realgar, to loosen the hairs. Other depilatories used are caustic soda, sulphide of sodium, calcium bisulphide, and various acid substances. After removal of the hairs, the skins pass to the tanner. Before they are treated by the fellmonger, the skins, fresh or dried, emit a faint odour. Decomposition is more pronounced in the lime-pits, where the smell is ammoniacal, a characteristic also of the waste lime, which has to be periodically removed. Ammoniacal gas liquor is in some cases used instead of the lime in the depilatory process. What is intended for sole leather is not limed, but is soaked until an ammoniacal odour is emitted. Some of the dried skins from abroad have previously been treated with arsenic, and it is said that arsenical vapours and hydrogen bisulphide are evolved when they are being prepared for tanning. Fellmongering is a public nuisance.

The main duties of the tanner are to place the skins in the tanning bath. and to turn them over periodically during their very extensive treatment. A faint odour comes from the tan pits, but what is its exact character is doubtful. As acetic fermentation takes place in the tanning bath, the reaction of which is acid, amine liberation must be small in degree. Tan itself has an odour. Preliminary to the tanning process, and after depilation, the skins are submitted to operations intended for the removal from them of lime, and for other purposes. These operations vary according to the nature of the hide and the kind of leather required, and they include the use of dogs', fowls', and pigeons' dung, and various acids (hydrochloric, sulphuric, lactic, formic). Tanneries are public nuisances owing to the emanations and the character of the waste water, but more, I think, because of the fellmongering part of the business. The premises are necessarily in a foul and dirty state, and decomposition of accumulated "fleshings" pared from the fresh skins, along with decomposition in the stored untreated hides, does not help matters.

I am without information of any characteristic ailments among tanners or fellmongers except that they are liable to ulcers and other sores on the hands caused by the action of lime and arsenic. The occupation is a healthy one, and the comparative mortality figure for all causes is small. and, as usual when this figure is small, the death-rate from cancer is low. This low death-rate from cancer and from all causes has been a source of difficulty to me. I am unable to give any valid explanation of the low cancer incidence in this occupational group, but the low death-rate from all causes encourages me in the belief that there is some factor undetermined. The small number of deaths from cancer during both periods lessens the probability that the comparative mortality figure for cancer is unreliable.

The furriers and skinners—some of the true fellmongers being here included—are not only exposed to the action of decomposition products, but also of arsenic which has been used for the preservation of foreign skins. The furriers also suffer from the effects of mercuric nitrate used for dressing the skins, the chronic effects including great debility; but, of course, we are waiting for proof that mercury is a potent agent.

Some only of the occupational groups occupying a somewhat lower average position than the above can now be dealt with. Of the few groups omitted here and there, it is impossible to gain information of any special factors such as those which we have before considered, or if such factors can be predicated, I am not satisfied that they will explain the higher incidence.

Plasterer, Whitewasher, Paperhanger [*Cancer*—71 (51), 64 (63); *Alcoholism*—17 (15), 26 (16)].—From our point of view this is a heterogeneous group. In the case of the two first occupations, lime will be a potent substance, for it can induce eczema as well as inflammatory conditions of the mucous membranes, even ulceration of the nose. Paperhangers suffer in various ways from the effects of arsenical compounds present in wallpapers.

Tool, Scissors, File, Saw, Needle—Maker [*Cancer*—67 (51), 67 (63); *Alcoholism*—14 (15), 9 (16)].—Though, in the Sheffield trades, water and watery solutions are used as tempering fluids, tempering is also performed in mixtures into which tallow, animal and mineral oils, pitch, and resin, among other substances, enter as components. In case-hardening are employed the horns and hoofs of cattle, leather, and animal and vegetable charcoal. Certain woods used for the hafts of knives have irritative effects upon skin and mucous membrane. The air of the grinding shops is laden with particles of steel, having sharp and jagged outlines, which irritate the throat and trachea; and much rouge, whiting, and powdered pumice pass into the air of the polishing-rooms. Cancer incidence is much higher in Sheffield than in the surrounding districts.

Costermonger, Hawker, Streetseller [*Cancer*—52 (51), 79 (63); *Alcoholism*—42 (15), 57 (16)].—Included in this group is a proportion of individuals of a somewhat degenerate type, and many of the conditions under which the members of the group live are debilitating. They are exposed to the inclemencies of the weather without enjoying to the full extent the safeguard of that activity which tends to neutralise the evil effects. The death-rate from alcoholism is very pronounced. Excessive use of the voice is one of the putative causes of throat cancer.

Plumber, Painter, Glazier [*Cancer*—61 (51), 69 (63); *Alcoholism*—15 (16), 12 (16)].—This is another heterogeneous group. The work of the plumber in sanitation and in connection with gas-supply may be operative. Painters suffer from irritation of the skin and mucous membrane, and from depressant conditions, caused by some or other of the media used: turpentine, wood naphtha, methylated spirit, and benzene. Those working in the confined spaces in ships may also suffer from hyperidrosis and affections of the hair. Bitumen and similar substances enter into the composition of special varnishes, but these are little used. As I have previously remarked, I am unable to ascribe potency to lead compounds.

Dock Labourer [*Cancer*—59 (51), 67 (63); *Alcoholism*—60 (15), 49 (16)].—Work is partly performed at the open-air sewage tanks known as docks and at the sides of polluted rivers; and the dock labourer usually resides near to his work. At the 1891 census, of 54,996 dock labourers in England and Wales, there were 14.562 in the registration county of London. There is a high death-rate from alcoholism.

Rope, Twine, Cord—Maker [*Cancer*—63 (51), 62 (63) ; *Alcoholism*—6 (15), 5 (16)].—Wood-tar is used for the preservation of ropes.

Shoemaker [*Cancer*—58 (51), 66 (63) ; *Alcoholism*—11 (15), 12 (16)].—Mineral oils, pitch from wood-tar, benzene, tallow, and animal oils are among the substances used in boot and shoe making. Already mentioned are those cases of cancer of the tongue in lathers which were due to its use in pushing nails out of the mouth ; this factor is here worth consideration. In boot repairers, pressure against the body induces dyspepsia and ulceration of the stomach, and they are liable to be constipated.

Messenger, Porter, &c. (*not Railway or Government*) [*Cancer*—55 (51), 79 (63); *Alcoholism*—18 (15), 32 (16)].—Out of 175,553 individuals composing this occupational group in 1891, no less than 52,775 were in the registration county of London.

CHAPTER XXV.

A Description of Some of the Suspected Chemical Agents.

MY readers will probably thank me for a brief account of some of the organic compounds mentioned in this book, and I will confine myself to such as are nitrogenous bases, in the belief that the most potent agents will be found amongst them.

Fatty Amines.—These are compound ammonias, and, therefore, are strong bases. One, two, or three atoms of hydrogen in ammonia are replaced by one, two, or three groups of atoms respectively of the homologous series—methyl, ethyl, propyl, &c.

Methylamine	$CH_2.NH_2$.	Ethylamine	$C_2H_5.NH_2$.
Dimethylamine ...	$(CH_2)_2.NH$.	Diethylamine......	$(C_2H_5)_2.NH$.
Trimethylamine ...	$(CH_2)_3.N$.	Triethylamine ...	$(C_2H_5)_3.N$.

Methylamine is the only gaseous fatty amine. The remainder are volatile liquids miscible with water, many with a lower specific gravity and boiling point than the latter, which it is important to note, for they will more readily pass from the soil into the air. The odour of some of them is described as ammoniacal, of others fishy.

Pyridine Bases.—These are aromatic amines, forming a homologous series, so that picoline, the second member of the series, is methyl-pyridine, of which there are three isomers, and lutidine, the third member, is dimethyl-pyridine, of which there are six isomers. The following are the known members of the series :—

		B.P.			B.P.
Pyridine.........	C_5H_5N.	115°.	Parvoline	$C_9H_{13}N$.	188°.
Picoline	C_6H_7N.	135°.	Coridine.........	$C_{10}H_{15}N$.	211°.
Lutidine.........	C_7H_9N.	155°.	Rubidine	$C_{11}H_{17}N$.	230°.
Collidine.........	$C_8H_{11}N$.	171°.	Viridine.........	$C_{12}H_{19}N$.	251°.

They are volatile liquids miscible with water, and the odour of pyridine is described as empyreumatic. Being strong bases and very stable, they fume with hydrochloric acid, forming additive compounds with it. Pyridine is the nucleus of many alkaloids, including nicotine.

Quinoline Bases.—Aromatic amines with a double benzene nucleus, and forming a homologous series, they are solids or volatile liquids, only slightly soluble in water, and are strong bases.

Quinoline (C_9H_7N. B.P. 239°) is the nucleus of many alkaloids, including strychnine and quinine.

Acridine Bases.—Acridine ($C_{13}H_8N$. M.P. 107°. B.P. 360°), the first member of a homologous series, is an aromatic amine with three benzene nuclei, but is not a very strong base. It crystallises in needles, and is sparingly soluble in cold water.

Aniline ($C_6H_5.NH_2$. B.P. 183°) is an aromatic amine with marked basic properties. A volatile oil, it is only slightly soluble in cold water. Toluidine is the next homologue in the series.

Nitrobenzene ($C_6H_5NO_2$. B.P. 209°) is a volatile oil insoluble in cold water.

Pyrrol (C_4H_5N. B.P. 133°), a very feeble base, is a cyclic compound. A volatile oil, it is insoluble in cold water.

Nicotine ($C_{10}H_{11}N$. B.P. 242°) is a volatile oil, a strong base, and is miscible with water.

Ptomaines.—The ptomaines form too diverse a group chemically, except in their basic nature, to render profitable a recapitulation of their properties. The oxygenated—neurine, choline, muscarine, &c.—are crystalline fatty compounds and powerful physiological agents. The non-oxygenated—volatile and odorous liquids—are fatty diamines (cadaverine, putrescine, or neuridine), which are weak agents physiologically, or they are aromatic monamines (isomers of parvoline, collidine, &c.), which are more powerful. The ptomaines have a high solubility in cold water.

Indol (C_8H_7N. M.P. 52°. B.P. 245°) and *Skatol* (C_9H_9N. M.P. 95°. B.P. 265°) are weak bases with disgusting odour. They crystallise in plates, and are not very soluble in cold water.

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